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NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
 NEWS 2 Jan 25 BLAST(R) searching in REGISTRY available in STN on the Web
 NEWS 3 Jan 29 FSTA has been reloaded and moves to weekly updates
 NEWS 4 Feb 01 DKILIT now produced by FIZ Karlsruhe and has a new update
 frequency
 NEWS 5 Feb 19 Access via Tymnet and SprintNet Eliminated Effective 3/31/02
 NEWS 6 Mar 08 Gene Names now available in BIOSIS
 NEWS 7 Mar 22 TOXLIT no longer available
 NEWS 8 Mar 22 TRCTHERMO no longer available
 NEWS 9 Mar 28 US Provisional Priorities searched with P in CA/CAPLUS
 and USPATFULL
 NEWS 10 Mar 28 LIPINSKI/CALC added for property searching in REGISTRY
 NEWS 11 Apr 02 PAPERCHEM no longer available on STN. Use PAPERCHEM2
 instead.
 NEWS 12 Apr 08 "Ask CAS" for self-help around the clock
 NEWS 13 Apr 09 BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS 14 Apr 09 ZDB will be removed from STN
 NEWS 15 Apr 19 US Patent Applications available in IFICDB, IFIPAT, and
 IFIUDB
 NEWS 16 Apr 22 Records from IP.com available in CAPLUS, HCAPLUS, and
 ZCAPLUS
 NEWS 17 Apr 22 BIOSIS Gene Names now available in TOXCENTER
 NEWS 18 Apr 22 Federal Research in Progress (FEDRIP) now available

 NEWS EXPRESS February 1 CURRENT WINDOWS VERSION IS V6.0d,
 CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
 AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 18:43:32 ON 01 MAY 2002

=> file medline, uspatful, dgene, embase, biotechds, frosti, fsta

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
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FILE 'MEDLINE' ENTERED AT 18:44:03 ON 01 MAY 2002

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=> s kininogen

L1 4339 KININOGEN

=> s angiogenesis

L2 90365 ANGIOGENESIS

=> s l2 and inhibition

L3 15312 L2 AND INHIBITION

=> s l3 and compositon

L4 5 L3 AND COMPOSITON

=> d l4 ti abs ibib tot

L4 ANSWER 1 OF 5 USPATFULL

TI Gene sequence variances in genes related to folate metabolism having utility in determining the treatment of disease

AB The present disclosure describes the use of genetic variance information

for folate transport or metabolism genes or pyrimidine transport or metabolism genes in the selection of effective methods of treatment of a

disease or condition. The variance information is indicative of the expected response of a patient to a method of treatment. Methods of determining relevant variance information and additional methods of using such variance information are also described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:72850 USPATFULL
TITLE: Gene sequence variances in genes related to folate
metabolism having utility in determining the treatment
of disease
INVENTOR(S): Stanton, Vincent P., JR., Belmont, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002039990	A1	20020404
APPLICATION INFO.:	US 2000-733651	A1	20001207 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2000-710768, filed on 8 Nov 2000, PENDING Continuation-in-part of Ser.		

No. US 2000-696634, filed on 24 Oct 2000, PENDING
Continuation-in-part of Ser. No. US 2000-684359, filed
on 6 Oct 2000, PENDING Continuation-in-part of Ser.

No. US 2000-638267, filed on 14 Aug 2000, PENDING
Continuation-in-part of Ser. No. US 2000-596033, filed
on 15 Jun 2000, ABANDONED Continuation-in-part of Ser.
No. US 1999-357743, filed on 20 Jul 1999, ABANDONED
Continuation-in-part of Ser. No. US 1999-357024, filed
on 19 Jul 1999, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-93484P	19980720 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	ANITA L. MEIKLEJOHN, PH.D., FISH & RICHARDSON P.C., 225	

Franklin Street, Boston, MA, 02110-2804

NUMBER OF CLAIMS: 119
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Page(s)
LINE COUNT: 7986
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 2 OF 5 USPATFULL

TI Anti-cancer therapy agent of arsenic hexoxide (As₄O₆) of a natural
chemical substance and its pharmaceutical composition
AB This invention is about the identification of the HD-2, a natural
chemical substance that was separated and purified from a natural
product, Sinsuk, as arsenic hexoxide (As_{sub.40.sub.6}) and about its
therapeutic efficacy as an anti-cancer drug and pharmaceutical
composition. Arsenic hexoxide (As_{sub.40.sub.6}), a natural chemical
substance obtained from Sinsuk after eliminating the toxic property,
has
a potent anti-cancer efficacy by its direct cytotoxicity on tumor cells
and suppresses the formation of new blood vessels of tumor masses,
which
results in complete cure of malignant cancers.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:48062 USPATFULL
TITLE: Anti-cancer therapy agent of arsenic hexoxide (As₄O₆)
of a natural chemical substance and its pharmaceutical
composition
INVENTOR(S): Bae, Ill-Ju, Seoul, KOREA, REPUBLIC OF
Kim, Jong-Bae, Pohang-city, KOREA, REPUBLIC OF
Eun, Choong-Ki, Pusan-city, KOREA, REPUBLIC OF
Song, Seung-Kyu, Pohang-city, KOREA, REPUBLIC OF
Suh, Byung-Sun, Pohang-city, KOREA, REPUBLIC OF
Lee, Kwan-Hee, Pohang-city, KOREA, REPUBLIC OF

Doo, Myoung-Sool, Pohang-city, KOREA, REPUBLIC OF
Kwak, Jin-Hwan, Pohang-city, KOREA, REPUBLIC OF
ong, Byung-Doo, Pohang-city, KOREA, REPUBLIC OF
Yoon, Taek-Joon, Koyang-city, KOREA, REPUBLIC OF
Kang, Tae-Bong, Pohang-city, KOREA, REPUBLIC OF
Park, Choon-Ho, Pohang-city, KOREA, REPUBLIC OF

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002028253	A1	20020307
APPLICATION INFO.:	US 2001-951393	A1	20010914 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1998-105086, filed on 26 Jun 1998, GRANTED, Pat. No. US 6309672		

	NUMBER	DATE
PRIORITY INFORMATION:	KR 1998-16486	19980508
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Gary M. Nath, Nath & Associates PLLC, 6th Floor, 1030 15th Street, N.W., Washington, DC, 20005	
NUMBER OF CLAIMS:	4	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	34 Drawing Page(s)	
LINE COUNT:	971	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		

L4 ANSWER 3 OF 5 USPATFULL
TI Somatostatin antagonists
AB The invention features somatostatin antagonists having a D-amino acid at
at the second residue.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2001:112494 USPATFULL
TITLE: Somatostatin antagonists
INVENTOR(S): Coy, David H., New Orleans, LA, United States
Morgan, Barry, Franklin, MA, United States
Murphy, William, Slidell, LA, United States
PATENT ASSIGNEE(S): Biomeasure Incorporated, Milford, MA, United States
(U.S. corporation)
The Administration of the Tulane Educational Fund, New Orleans, LA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6262229	B1	20010717
APPLICATION INFO.:	US 1997-855204		19970513 (8)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-32358P	19961204 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Cintins, Marianne M.	
ASSISTANT EXAMINER:	Delacroix-Muirheid, C.	
LEGAL REPRESENTATIVE:	Conway, John D., Morrill, Brian R. Fish & Richardson	
NUMBER OF CLAIMS:	10	
EXEMPLARY CLAIM:	1	
LINE COUNT:	1228	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		

L4 ANSWER 4 OF 5 USPATFULL
TI Urokinase-type plasminogen activator receptor

AB Activation of plasminogen to plasmin is inhibited by preventing the binding of a receptor binding form of urokinase-type plasminogen activator to a urokinase-type plasminogen activator receptor in a mammal, thereby preventing the urokinase-type plasminogen activator from converting plasminogen into plasmin. DNA fragments which encode for soluble, active fragments of the urokinase-type plasminogen activator receptor are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2001:93478 USPATFULL
TITLE: Urokinase-type plasminogen activator receptor
INVENTOR(S): Dan.o slashed. , Keld, Charlottenlund, Denmark
 Blasi, Francesco, Charlottenlund, Denmark
 Roldan, Ann Louring, Vallensb.ae butted.k, Denmark
 Cubellis, Maria Vittoria, Naples, Italy
 Masucci, Maria Teresa, Naples, Italy
 Appella, Ettore, Chevy Chase, MD, United States
 Schleuning, W.D., Berlin, Germany, Federal Republic of
 Behrendt, Niels, Bagsv.ae butted.rd, Denmark
 R.o slashed.nne, Ebbe, Copenhagen, Denmark
 Kristensen, Peter, Copenhagen, Denmark
 Pollanen, Jari, Espoo, Finland
 Salonen, Eeva-Marjatta, Espoo, Finland
 Stephens, Ross W., Vantaa, Finland
 Tapiovaara, Hannele, Helsinki, Finland
 Vaheri, Antti, Kauniainen, Finland
 M.o slashed.ller, Lisbeth Birk, Bagsv.ae butted.rd, Denmark
 Ellis, Vincent, Copenhagen, Denmark
 Lund, Leif R.o slashed.ge, Copenhagen, Denmark
 Ploug, Michael, Copenhagen, Denmark
 Pyke, Charles, S.o slashed.borg, Denmark
 Patthy, Laszlo, Budapest, Hungary
PATENT ASSIGNEE(S): Cancerforskningsfondet af 1989, Denmark (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6248712	B1	20010619
APPLICATION INFO.:	US 1995-442108		19950516 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1994-319052, filed on 6 Oct 1994, now patented, Pat. No. US 5891644 Continuation of Ser. No. US 824189, now abandoned Continuation-in-part of Ser. No. US 1989-374854, filed on 3 Jul 1989, now abandoned Continuation-in-part of Ser. No. US 1989-334613, filed on 7 Apr 1989, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Feisee, Lila		
ASSISTANT EXAMINER:	Basi, Nirmal S.		
LEGAL REPRESENTATIVE:	Cooper, Iver P.		
NUMBER OF CLAIMS:	28		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	86 Drawing Figure(s); 54 Drawing Page(s)		
LINE COUNT:	6444		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 5 OF 5 USPATFULL

TI Vectors and methods for recombinant production of uPA-binding fragments of the human urokinase-type plasminogen receptor (uPAR)
AB Activation of plasminogen to plasma is inhibited by preventing the binding of a receptor binding form of urokinase-type plasminogen

activator to a urokinase-type plasminogen activator receptor in a mammal, thereby preventing the urokinase-type plasminogen activator from converting plasminogen into plasmin. DNA fragments which encode for soluble, active fragments of the urokinase-type plasminogen activator are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 1999:43412 USPATFULL

TITLE: Vectors and methods for recombinant production of uPA-binding fragments of the human urokinase-type plasminogen receptor (uPAR)

INVENTOR(S): Dan.o slashed. , Keld, Charlottenlund, Denmark
Blasi, Francesco, Charlottenlund, Denmark
Roldan, Ann Louring, Vallensb.ae butted.k, Denmark
Cubellis, Maria Vittoria, Napoli, Italy
Masucci, Maria Teresa, Napoli, Italy
Appella, Ettore, Chevy Chase, MD, United States
Schleuning, Wolf-Dieter, Berlin, Germany, Federal Republic of
Behrendt, Niels, Bagsv.ae butted.rd, Denmark
R.o slashed.nne, Ebbe, Copenhagen, Denmark
Kristensen, Peter, Copenhagen, Denmark
Pollanen, Jari, Espoo, Finland
Salonen, Eeva-Marjatta, Espoo, Finland
Stephens, Ross W., Helsinki, Finland
Tapiovaara, Hannele, Helsinki, Finland
Vaheri, Antti, Kauniainen, Finland
M.o slashed.ller, Lisbeth Birk, Bagsv.ae butted.rd, Denmark
Ellis, Vincent, Copenhagen, Denmark
Lund, Leif R.o slashed.ge, Copenhagen, Denmark
Ploug, Michael, Copenhagen, Denmark
Pyke, Charles, S.o slashed.borg, Denmark
Patthy, Laszlo, Budapest, Hungary
PATENT ASSIGNEE(S): Cancerforskningsfondet af 1989, Copenhagen K, Denmark (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5891664		19990406
APPLICATION INFO.:	US 1994-319052		19941006 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1991-824189, filed on 6 Dec 1991, now abandoned which is a continuation-in-part of Ser. No. US 1989-374854, filed on 3 Jul 1989, now abandoned which is a continuation-in-part of Ser. No. US 1989-334613, filed on 7 Apr 1989, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Walsh, Stephen G.		
ASSISTANT EXAMINER:	Fitzgerald, David L.		
LEGAL REPRESENTATIVE:	Cooper, Iver P.		
NUMBER OF CLAIMS:	22		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	83 Drawing Figure(s); 53 Drawing Page(s)		
LINE COUNT:	6449		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

(FILE 'HOME' ENTERED AT 18:43:32 ON 01 MAY 2002)

FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, BIOTECHDS, FROSTI, FSTA'
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AT 18:44:03 ON 01 MAY 2002

L1 4339 S KININOGEN
L2 90365 S ANGIOGENESIS
L3 15312 S L2 AND INHIBITION
L4 5 S L3 AND COMPOSITON

=> s l3 and composition

L5 2358 L3 AND COMPOSITION

=> s l5 and glycine

L6 890 L5 AND GLYCINE

=> s l7 and histidine

L7 NOT FOUND

The L-number entered could not be found. To see the definition
of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s l6 and histidine

L7 468 L6 AND HISTIDINE

=> s l7 and lysine

L8 424 L7 AND LYSINE

=> s l8 and PHE

L9 295 L8 AND PHE

=> s l9 and protecting group

L10 53 L9 AND PROTECTING GROUP

=> d l10 ti abs ibib 1-10

L10 ANSWER 1 OF 53 USPATFULL

TI .beta.-sheet mimetics and methods relating to the use thereof
AB .beta.-sheet mimetics and methods relating to the same are disclosed.
The .beta.-sheet mimetics have utility as protease and kinase
inhibitors, as well as inhibitors of transcription factors and
protein-protein binding interactions. Methods of the invention include
administration of a .beta.-sheet mimetic, or use of the same for the
manufacture of a medicament for treatment of a variety of conditions
associated with the targeted protease, kinase, transcription factor
and/or protein-protein binding interaction.

ACCESSION NUMBER: 2002:81487 USPATFULL
TITLE: .beta.-sheet mimetics and methods relating to the use
thereof
INVENTOR(S): Qabar, Maher N., Redmond, WA, United States
McMillan, Michael K., Bellevue, WA, United States
Kahn, Michael S., Kirkland, WA, United States
Tulinsky, John E., Seattle, WA, United States
Ogbu, Cyprian O., Bellevue, WA, United States
Mathew, Jessymol, Bellevue, WA, United States
PATENT ASSIGNEE(S): Molecumetics Ltd., Bellevue, WA, United States (U.S.
corporation)

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NEWS	4	Feb 24 TEMA now available on STN
NEWS	5	Feb 26 NTIS now allows simultaneous left and right truncation
NEWS	6	Feb 26 PCTFULL now contains images
NEWS	7	Mar 04 SDI PACKAGE for monthly delivery of multifile SDI results
NEWS	8	Mar 24 PATDPAFULL now available on STN
NEWS	9	Mar 24 Additional information for trade-named substances without structures available in REGISTRY
NEWS	10	Apr 11 Display formats in DGENE enhanced
NEWS	11	Apr 14 MEDLINE Reload
NEWS	12	Apr 17 Polymer searching in REGISTRY enhanced
NEWS	13	AUG 22 Indexing from 1927 to 1936 added to records in CA/CAPLUS
NEWS	14	Apr 21 New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS	15	Apr 28 RDISCLOSURE now available on STN
NEWS	16	May 05 Pharmacokinetic information and systematic chemical names added to PHAR
NEWS	17	May 15 MEDLINE file segment of TOXCENTER reloaded
NEWS	18	May 15 Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS	19	May 19 Simultaneous left and right truncation added to WSCA
NEWS	20	May 19 RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS	21	Jun 06 Simultaneous left and right truncation added to CBNB
NEWS	22	Jun 06 PASCAL enhanced with additional data
NEWS	23	Jun 20 2003 edition of the FSTA Thesaurus is now available
NEWS	24	Jun 25 HSDB has been reloaded
NEWS	25	Jul 16 Data from 1960-1976 added to RDISCLOSURE
NEWS	26	Jul 21 Identification of STN records implemented
NEWS	27	Jul 21 Polymer class term count added to REGISTRY
NEWS	28	Jul 22 INPADOC: Basic index (/BI) enhanced; Simultaneous Left and Right Truncation available
NEWS	29	AUG 05 New pricing for EUROPATFULL and PCTFULL effective August 1, 2003
NEWS	30	AUG 13 Field Availability (/FA) field enhanced in BEILSTEIN
NEWS	31	AUG 15 PATDPAFULL: one FREE connect hour, per account, in September 2003
NEWS	32	AUG 15 PCTGEN: one FREE connect hour, per account, in September 2003
NEWS	33	AUG 15 RDISCLOSURE: one FREE connect hour, per account, in September 2003
NEWS	34	AUG 15 TEMA: one FREE connect hour, per account, in September 2003
NEWS	35	AUG 18 Data available for download as a PDF in RDISCLOSURE
NEWS	36	AUG 18 Simultaneous left and right truncation added to PASCAL
NEWS	37	AUG 18 FROSTI and KOSMET enhanced with Simultaneous Left and Right Truncation

COLLINS-RACIE, LISA A., ACTON, MA, UNITED STATES
 MERBERG, DAVID, ACTON, MA, UNITED STATES
 AGOSTINO, MICHAEL J., ANDOVER, MA, UNITED STATES
 STEININGER, ROBERT, II, CAMBRIDGE, MA, UNITED STATES
 SPAULDING, VIKKI, BILLERICA, MA, UNITED STATES
 WONG, GORDON G., BROOKLINE, MA, UNITED STATES
 CLARK, HILARY F., SAN FRANCISCO, CA, UNITED STATES
 FECHTEL, KIM, ARLINGTON, MA, UNITED STATES
 EVANS, CHERYL, GERMANTOWN, MD, UNITED STATES
 TREACY, MAURICE, DUBLIN, IRELAND

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003096951	A1	20030522
APPLICATION INFO.:	US 1999-374046	A1	19990813 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-96622P	19980814 (60)
	US 1998-96815P	19980817 (60)
	US 1998-99229P	19980904 (60)
	US 1998-105368P	19981023 (60)
	US 1999-115234P	19990108 (60)
	US 1999-119931P	19990212 (60)
	US 1999-120575P	19990218 (60)
	US 1999-132020P	19990430 (60)
	US 1999-148424P	19990811 (60)

DOCUMENT TYPE: Utility
 FILE SEGMENT: APPLICATION
 LEGAL REPRESENTATIVE: LAHIVE & COCKFIELD, 28 STATE STREET, BOSTON, MA, 02109
 NUMBER OF CLAIMS: 13
 EXEMPLARY CLAIM: 1
 NUMBER OF DRAWINGS: 3 Drawing Page(s)
 LINE COUNT: 22385
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 2 OF 13 USPATFULL on STN

TI Novel human leucine-rich repeat containing protein expressed predominately in small intestine, HLRRS11

AB The present invention provides novel polynucleotides encoding HLRRS11 polypeptides, fragments and homologues thereof. Also provided are vectors, host cells, antibodies, and recombinant and synthetic methods for producing said polypeptides. The invention further relates to diagnostic and therapeutic methods for applying these novel HLRRS11 polypeptides to the diagnosis, treatment, and/or prevention of various diseases and/or disorders related to these polypeptides, particularly gastrointestinal diseases and/or disorders. The invention further relates to screening methods for identifying agonists and antagonists of the polynucleotides and polypeptides of the present invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2003:23722 USPATFULL

TITLE: Novel human leucine-rich repeat containing protein expressed predominately in small intestine, HLRRS11

INVENTOR(S): Feder, John N., Belle Mead, NJ, UNITED STATES
 Ramanathan, Chandra S., Wallingford, CT, UNITED STATES
 Mintier, Gabriel A., Hightstown, NJ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003017562	A1	20030123
APPLICATION INFO.:	US 2001-29347	A1	20011220 (10)

NUMBER	DATE
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PRIORITY INFORMATION: US 2000-257774P 20001222 (60)
 DOCUMENT TYPE: Utility
 FILE SEGMENT: APPLICATION
 LEGAL REPRESENTATIVE: STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT
 DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000
 NUMBER OF CLAIMS: 23
 EXEMPLARY CLAIM: 1
 NUMBER OF DRAWINGS: 9 Drawing Page(s)
 LINE COUNT: 14217
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 3 OF 13 USPATFULL on STN
 TI 31 human secreted proteins
 AB The present invention relates to novel human secreted proteins and
 isolated nucleic acids containing the coding regions of the genes
 encoding such proteins. Also provided are vectors, host cells,
 antibodies, and recombinant methods for producing human secreted
 proteins. The invention further relates to diagnostic and therapeutic
 methods useful for diagnosing and treating disorders related to these
 novel human secreted proteins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2003:4280 USPATFULL
 TITLE: 31 human secreted proteins
 INVENTOR(S): Rosen, Craig A., Laytonsville, MD, UNITED STATES
 Ruben, Steven M., Olney, MD, UNITED STATES
 Ferrie, Ann M., Tewksbury, MA, UNITED STATES
 Florence, Charles, Rockville, MD, UNITED STATES
 Young, Paul E., Gaithersburg, MD, UNITED STATES
 Yu, Guo-Liang, Berkeley, CA, UNITED STATES
 Ni, Jian, Rockville, MD, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003004324	A1	20030102
APPLICATION INFO.:	US 2001-798889	A1	20010306 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1999-393022, filed on 9 Sep 1999, ABANDONED Continuation-in-part of Ser. No. WO 1999-US5721, filed on 11 Mar 1999, UNKNOWN		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-77714P	19980312 (60)
	US 1998-77686P	19980312 (60)
	US 1998-77687P	19980312 (60)
	US 1998-77696P	19980312 (60)

DOCUMENT TYPE: Utility
 FILE SEGMENT: APPLICATION
 LEGAL REPRESENTATIVE: HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE,
 ROCKVILLE, MD, 20850

NUMBER OF CLAIMS: 23
 EXEMPLARY CLAIM: 1
 LINE COUNT: 12188

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 4 OF 13 USPATFULL on STN
 TI Compositions and methods relating to lung specific genes and proteins
 AB The present invention relates to newly identified nucleic acids and
 polypeptides present in normal and neoplastic lung cells, including
 fragments, variants and derivatives of the nucleic acids and
 polypeptides. The present invention also relates to antibodies to the
 polypeptides of the invention, as well as agonists and antagonists of
 the polypeptides of the invention. The invention also relates to

compositions comprising the nucleic acids, polypeptides, antibodies, variants, derivatives, agonists and antagonists of the invention and methods for the use of these compositions. These uses include identifying, diagnosing, monitoring, staging, imaging and treating lung cancer and non-cancerous disease states in lung, identifying lung tissue, monitoring and identifying and/or designing agonists and antagonists of polypeptides of the invention. The uses also include gene therapy, production of transgenic animals and cells, and production of engineered lung tissue for treatment and research.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:323329 USPATFULL
TITLE: Compositions and methods relating to lung specific genes and proteins
INVENTOR(S): Macina, Roberto, San Jose, CA, UNITED STATES
Recipon, Herve A., San Francisco, CA, UNITED STATES
Chen, Sei-Yu, Foster City, CA, UNITED STATES
Sun, Yongming, San Jose, CA, UNITED STATES
Liu, Chenghua, San Jose, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002183500	A1	20021205
APPLICATION INFO.:	US 2001-1857	A1	20011120 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-252054P	20001120 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	LICATLA & TYRRELL P.C., 66 E. MAIN STREET, MARLTON, NJ, 08053	
NUMBER OF CLAIMS:	17	
EXEMPLARY CLAIM:	1	
LINE COUNT:	9589	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 5 OF 13 USPATFULL on STN
TI 23927, a novel human ion channel
AB The invention provides isolated nucleic acids molecules, designated 23927 or IC23927 nucleic acid molecules, which encode ion channel molecules. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing IC23927 nucleic acid molecules, host cells into which the expression vectors have been introduced, and nonhuman transgenic animals in which an IC23927 gene has been introduced or disrupted. The invention still further provides isolated IC23927 proteins, fusion proteins, antigenic peptides and anti-IC23927 antibodies. Diagnostic methods utilizing compositions of the invention are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:308330 USPATFULL
TITLE: 23927, a novel human ion channel
INVENTOR(S): Curtis, Rory A. J., Southborough, MA, UNITED STATES
Silos-Santiago, Inmaculada, Cambridge, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002173455	A1	20021121
APPLICATION INFO.:	US 2001-796720	A1	20010228 (9)

NUMBER	DATE
--------	------

PRIORITY INFORMATION: US 2000-185938P 20000229 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: LAHIVE & COCKFIELD, 28 STATE STREET, BOSTON, MA, 02109
NUMBER OF CLAIMS: 34
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Page(s)
LINE COUNT: 5097
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 6 OF 13 USPATFULL on STN

TI CD16-II variants

AB Human CD16-II variants, DNA sequences coding for them, their use in therapy and/or in diagnosis of autoimmune diseases and inflammatory illnesses, as well as pharmaceutical compositions comprising them, are disclosed. The sequence listing for the new polypeptides is provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:224701 USPATFULL
TITLE: CD16-II variants
INVENTOR(S): Luo, Shun, Needham, MA, United States
PATENT ASSIGNEE(S): Applied Research Systems ARS Holding N.V., NETHERLANDS ANTILLES (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6444789	B1	20020903
APPLICATION INFO.:	US 1995-433123		19950503 (8)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Ulm, John		
LEGAL REPRESENTATIVE:	Browdy and Neimark, P.L.L.C.		
NUMBER OF CLAIMS:	10		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	7 Drawing Figure(s); 7 Drawing Page(s)		
LINE COUNT:	1004		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 7 OF 13 USPATFULL on STN

TI Secreted proteins and polynucleotides encoding them

AB Novel polynucleotides and the proteins encoded thereby are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:126876 USPATFULL
TITLE: Secreted proteins and polynucleotides encoding them
INVENTOR(S): Jacobs, Kenneth, Newton, MA, UNITED STATES
McCoy, John M., Reading, MA, UNITED STATES
LaVallie, Edward R., Harvard, MA, UNITED STATES
Collins-Racie, Lisa A., Acton, MA, UNITED STATES
Evans, Cheryl, Germantown, MD, UNITED STATES
Merberg, David, Acton, MA, UNITED STATES
Treacy, Maurice, Dun Laoghaire, IRELAND
Spaulding, Vikki, Lowell, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002065394	A1	20020530
APPLICATION INFO.:	US 2000-745763	A1	20001222 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1998-40963, filed on 18 Mar 1998, UNKNOWN		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	LAHIVE & COCKFIELD, 28 STATE STREET, BOSTON, MA, 02109		
NUMBER OF CLAIMS:	264		

EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Page(s)
LINE COUNT: 17713
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 8 OF 13 USPATFULL on STN

TI Size-variable strain-specific protective antigen for potomac horse fever
AB An isolated and purified antigen which is expressed by a wild-type E. risticii strain and is specific to the strain. The present invention also relates to nucleic acid constructs which encode the antigen, expression vectors, transformed host cells, and methods for producing the antigen.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:87998 USPATFULL
TITLE: Size-variable strain-specific protective antigen for potomac horse fever
INVENTOR(S): Dutta, Sukanta, Glenn Dale, MD, United States
Biswas, Biswajit, Greenbelt, MD, United States
Vemulapalli, Ramesh, Blacksburg, VA, United States
PATENT ASSIGNEE(S): University of Maryland College Park, College Park, MD, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6375954	B1	20020423
APPLICATION INFO.:	US 1998-157257		19980918 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-59252P	19970918 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Graser, Jennifer E.	
LEGAL REPRESENTATIVE:	Arent Fox Kintner Plotkin Kahn PLLC	
NUMBER OF CLAIMS:	3	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	13 Drawing Figure(s); 14 Drawing Page(s)	
LINE COUNT:	2907	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 9 OF 13 USPATFULL on STN

TI Cell division regulators
AB The invention provides three human cell division regulators (HCDR) and polynucleotides which identify and encode HCDR. The invention also provides expression vectors, host cells, agonists, antibodies and antagonists. The invention also provides methods for preventing and treating disorders associated with expression of HCDR.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2000:124797 USPATFULL
TITLE: Cell division regulators
INVENTOR(S): Hillman, Jennifer L., Mountain View, CA, United States
Bandman, Olga, Mountain View, CA, United States
Lal, Preeti, Sunnyvale, CA, United States
Shah, Purvi, Sunnyvale, CA, United States
Corley, Neil C., Mountain View, CA, United States
PATENT ASSIGNEE(S): Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6121019		20000919
APPLICATION INFO.:	US 1999-274570		19990323 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1998-165234, filed on 1 Oct 1998, now patented, Pat. No. US 5928899 which is a division of Ser. No. US 1997-951148, filed on 15 Oct 1997, now patented, Pat. No. US 5871973

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Achutamurthy, Ponnathapu
ASSISTANT EXAMINER: Mayhew, Bradley S.
LEGAL REPRESENTATIVE: Incyte Pharmaceuticals, Inc.
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 26 Drawing Figure(s); 26 Drawing Page(s)
LINE COUNT: 3015
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 10 OF 13 USPATFULL on STN

TI Zinc ring protein

AB The invention provides a human zinc RING protein (ZIRI) and polynucleotides which identify and encode ZIRI. The invention also provides expression vectors, host cells, agonists, antibodies and antagonists. The invention also provides methods for treating disorders associated with expression of ZIRI.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 1999:159988 USPATFULL
TITLE: Zinc ring protein
INVENTOR(S): Hillman, Jennifer L., Mountain View, CA, United States
Lal, Preeti, Sunnyvale, CA, United States
Shah, Purvi, Sunnyvale, CA, United States
PATENT ASSIGNEE(S): Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5998372		19991207
APPLICATION INFO.:	US 1998-128369		19980803 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1997-867057, filed on 2 Jun 1997, now patented, Pat. No. US 5840555, issued on 24 Nov 1998		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Wax, Robert A.
ASSISTANT EXAMINER: Monshipouri, Maryam
LEGAL REPRESENTATIVE: Incyte Pharmaceuticals, Inc., Mohan-Peterson, Sheela
NUMBER OF CLAIMS: 2
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 9 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 2338
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 11 OF 13 USPATFULL on STN

TI CD16-II variants

AB Human CD16-II variants, DNA sequences coding for them, their use in therapy and/or in diagnosis of autoimmune diseases and inflammatory illnesses, as well as pharmaceutical compositions comprising them, are disclosed. The sequence listing for the new polypeptides is provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 1999:159782 USPATFULL
TITLE: CD16-II variants
INVENTOR(S): Luo, Shun, Needham, MA, United States
PATENT ASSIGNEE(S): Applied Research Systems ARS Holding N.V., Curacao, Netherlands (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5998166		19991207
APPLICATION INFO.:	US 1996-667939		19960624 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1995-433123, filed on 3 May 1995		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Hutzell, Paula K.		
ASSISTANT EXAMINER:	Lazar-Wesley, Elaine		
LEGAL REPRESENTATIVE:	Browdy and Neimark		
NUMBER OF CLAIMS:	8		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 7 Drawing Page(s)		
LINE COUNT:	1143		
CAS INDEXING IS AVAILABLE FOR THIS PATENT.			

L2 ANSWER 12 OF 13 USPATFULL on STN

TI Polynucleotides encoding human brain phosphodiesterase

AB Isolated cDNA clones from human brain (frontal cortex) cDNA libraries that encode a unique subtype of the low K_{sub.m}, cAMP-specific phosphodiesterases (PDE IVs) are disclosed. Analysis of the distribution of hPDE IV_{sub.B} mRNA expression in various human tissues using a nonconserved fragment of the cDNA as a probe revealed a restricted pattern of expression, with an .about.4-kb mRNA detected in brain, heart, lung and skeletal muscle and not in placenta, liver, kidney or pancreas. Furthermore, an additional .about.5-kb hPDE IV_{sub.B}^{sup.}-related mRNA species was detected in brain tissue. Expression of hPDE IV_{sub.B} in a genetically-engineered PDE-deficient strain of the yeast *Saccharomyces cerevisiae* resulted in the overproduction of cAMP PDE activity which displayed the expected kinetic characteristics for a PDE IV: 1) low K_{sub.m} (4.3 .mu.M) for cAMP, 2) high K_{sub.m} (>3 mM) for cGMP, and 3) sensitivity to rolipram (K_{sub.i} = 0.085 .mu.M), a selective inhibitor of PDE IV. Recombinant HPDE IV_{sub.B} also bound [³H]R-rolipram saturably and with a high affinity. Analysis of [³H]R-rolipram binding data revealed curvilinear Scatchard plots, suggesting the presence of two non-interacting high affinity rolipram binding sites (K_{sub.d} = 0.4 and 6 nM) or a negatively cooperative interaction among multiple binding sites. This novel enzyme is particularly useful for screening candidate compounds for their ability to serve as potential anti-depressant, antiasthmatic or anti-inflammatory agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 1999:89054 USPATFULL

TITLE: Polynucleotides encoding human brain phosphodiesterase

INVENTOR(S): Livi, George P., Havertown, PA, United States
McLaughlin, Megan M., Drexel Hill, PA, United States
Torphy, Theodore J., Bryn Mawr, PA, United States

PATENT ASSIGNEE(S): SmithKline Beecham Corporation, Philadelphia, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5932477		19990803
APPLICATION INFO.:	US 1997-942521		19971002 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 446386		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Elliott, George C.		
ASSISTANT EXAMINER:	Brusca, John S.		
LEGAL REPRESENTATIVE:	Hecht, Elizabeth T., Gimmi, Edward R., King, William T.		
NUMBER OF CLAIMS:	18		
EXEMPLARY CLAIM:	1		

NUMBER OF DRAWINGS: 7 Drawing Figure(s); 9 Drawing Page(s)
LINE COUNT: 1649
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 13 OF 13 USPATFULL on STN
TI Cell division regulators
AB The invention provides three human cell division regulators (HCDR) and polynucleotides which identify and encode HCDR. The invention also provides expression vectors, host cells, agonists, antibodies and antagonists. The invention also provides methods for preventing and treating disorders associated with expression of HCDR.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 1999:85250 USPATFULL
TITLE: Cell division regulators
INVENTOR(S): Hillman, Jennifer L., Mountain View, CA, United States
Bandman, Olga, Mountain View, CA, United States
Lal, Preeti, Sunnyvale, CA, United States
Shah, Purvi, Sunnyvale, CA, United States
Corley, Neil C., Mountain View, CA, United States
PATENT ASSIGNEE(S): Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5928899		19990727
APPLICATION INFO.:	US 1998-165234		19981001 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1997-951148, filed on 15 Oct 1997		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Wax, Robert A.		
ASSISTANT EXAMINER:	Mayhew, Bradley S.		
LEGAL REPRESENTATIVE:	Incyte Pharmaceuticals, Inc.		
NUMBER OF CLAIMS:	11		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	26 Drawing Figure(s); 26 Drawing Page(s)		
LINE COUNT:	2866		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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 NEWS 7 May 07 DGENE Reload
 NEWS 8 Jun 20 Published patent applications (A1) are now in USPATFULL
 NEWS 9 JUL 13 New SDI alert frequency now available in Derwent's
 DPWI and DPCI

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 AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2001

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=> s angiogenesis

L1 111516 ANGIOGENESIS

=> s l1 and inhibition

L2 20392 L1 AND INHIBITION

=> s l2 and peptide

L3 6317 L2 AND PEPTIDE

=> s kininogen

L4 10807 KININOGEN

=> s l3 and l4

L5 19 L3 AND L4

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L19 NOT FOUND

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L5 ANSWER 1 OF 19 MEDLINE

TI Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and inhibits **angiogenesis**: partial activity within domain 5.

AB We previously reported that the binding of two-chain high molecular weight

kininogen (HKa) to endothelial cells may occur through interactions with endothelial urokinase receptors. Since the binding of urokinase to urokinase receptors activates signaling responses and may stimulate mitogenesis, we assessed the effect of HKa binding on endothelial cell proliferation. Unexpectedly, HKa inhibited proliferation in response to several growth factors, with 50% **inhibition** caused by approximately 10 nM HKa. This activity was Zn(2+) dependent and not shared by either single-chain high molecular weight **kininogen** (HK) or low molecular weight **kininogen**. HKa selectively inhibited the proliferation of human umbilical vein and dermal microvascular endothelial cells, but did not affect that of umbilical vein

or human aortic smooth muscle cells, trophoblasts, fibroblasts, or carcinoma cells. **Inhibition** of endothelial proliferation by HKa was associated with endothelial cell apoptosis and unaffected by antibodies that block the binding of HK or HKa to any of their known endothelial receptors. Recombinant HK domain 5 displayed activity similar to that of HKa. In vivo, HKa inhibited neovascularization of subcutaneously implanted Matrigel plugs, as well as rat corneal **angiogenesis**. These results demonstrate that HKa is a novel inhibitor of **angiogenesis**, whose activity is dependent on the unique conformation of the two-chain molecule.

ACCESSION NUMBER: 2001111838 MEDLINE

DOCUMENT NUMBER: 20553282 PubMed ID: 11099478

TITLE: Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and inhibits **angiogenesis**: partial activity within domain 5.

AUTHOR: Zhang J C; Claffey K; Sakthivel R; Darzynkiewicz Z; Shaw D E; Leal J; Wang Y C; Lu F M; McCrae K R

CORPORATE SOURCE: Hematology-Oncology Division, Case Western Reserve University, School of Medicine, Cleveland, Ohio 44106-4937,

USA.

CONTRACT NUMBER: CA83134 (NCI)
HL50827 (NHLBI)

SOURCE: FASEB JOURNAL, (2000 Dec) 14 (15) 2589-600.
Journal code: FAS. ISSN: 0892-6638.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200102

ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered PubMed: 20010205
Entered Medline: 20010208

L5 ANSWER 2 OF 19 MEDLINE

TI Domain 5 of high molecular weight **kininogen** (kininostatin)

down-regulates endothelial cell proliferation and migration and inhibits **angiogenesis**.

AB We have demonstrated that high molecular weight **kininogen** (HK) binds specifically on endothelial cells to domain 2/3 of the urokinase receptor (uPAR). **Inhibition** by vitronectin suggests that kallikrein-cleaved HK (HKa) is antiadhesive. Plasma kallikrein bound to

HK cleaves prourokinase to urokinase, initiating cell-associated fibrinolysis. We postulated that HK cell binding domains would inhibit **angiogenesis**. We found that recombinant domain 5 (D5) inhibited endothelial cell migration toward vitronectin 85% at 0.27 microM with an IC(50) (concentration to yield 50% **inhibition**) = 0.12 microM. A D5 **peptide**, G486-K502, showed an IC(50) = 0.2 microM, but a 25-mer **peptide** from a D3 cell binding domain only inhibited migration 10% at 139 microM (IC(50) > 50 microM). D6 exhibited weaker inhibitory activity (IC(50) = 0.50 microM). D5 also potently inhibited endothelial cell proliferation with an IC(50) = 30 nM, while D3 and D6 were inactive. Using deletion mutants of D5, we localized the smallest region for full activity to H441-D474. To further map the active region, we created a molecular homology model of D5 and designed a series of peptides displaying surface loops. **Peptide** 440-455 was the most potent (IC(50) = 100 nM) in inhibiting proliferation but did not inhibit migration. D5 inhibited **angiogenesis** stimulated by fibroblast growth factor FGF2 (97%) in a chicken chorioallantoic membrane assay at 270 nM, and **peptide** 400-455 was also inhibitory (79%). HK D5 (for which we suggest the designation, "kininostatin") is a potent inhibitor of endothelial cell migration and proliferation in vitro and of **angiogenesis** in vivo. (Blood. 2000;95:543-550)

ACCESSION NUMBER: 2000094677 MEDLINE

DOCUMENT NUMBER: 20094677 PubMed ID: 10627460

TITLE: Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and inhibits **angiogenesis**.

AUTHOR: Colman R W; Jameson B A; Lin Y; Johnson D; Mousa S A

CORPORATE SOURCE: Sol Sherry Thrombosis Research Center, Temple University School of Medicine, Philadelphia, PA 19140, USA.. colmanr@astro.temple.edu

CONTRACT NUMBER: PO1HL56914 (NHLBI)
RO1CA63938 (NCI)

SOURCE: BLOOD, (2000 Jan 15) 95 (2) 543-50.
Journal code: A8G; 7603509. ISSN: 0006-4971.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200002

ENTRY DATE: Entered STN: 20000209
Last Updated on STN: 20000209
Entered Medline: 20000203

L5 ANSWER 3 OF 19 BIOSIS COPYRIGHT 2001 BIOSIS

TI Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and inhibits **angiogenesis**.

AB We have demonstrated that high molecular weight **kininogen** (HK) binds specifically on endothelial cells to domain 2/3 of the urokinase receptor (uPAR). **Inhibition** by vitronectin suggests that kallikrein-cleaved HK (HKa) is antiadhesive. Plasma kallikrein bound to

HK cleaves prourokinase to urokinase, initiating cell-associated fibrinolysis. We postulated that HK cell binding domains would inhibit **angiogenesis**. We found that recombinant domain 5 (D5) inhibited endothelial cell migration toward vitronectin 85% at 0.27 muM with an

IC50

(concentration to yield 50% inhibition) = 0.12 μ M. A D5 peptide, G486-K502, showed an IC50 = 0.2 μ M, but a 25-mer peptide from a D5 cell binding domain only inhibited migration 10% at 139 μ M (IC50 > 50 μ M). D6 exhibited weaker inhibitory activity (IC50 = 0.50 μ M). D5 also potentially inhibited endothelial cell proliferation with an IC50 = 30 nM, while D3 and D6 were inactive. Using deletion mutants of D5, we localized the smallest region for full activity to H441-D474. To further map the active region, we created a molecular homology model of D5 and designed a series of peptides displaying surface loops. Peptide 440-455 was the most potent (IC50 = 100 nM) in inhibiting proliferation but did not inhibit migration. D5 inhibited angiogenesis stimulated by fibroblast growth factor FGF2 (97%) in a chicken chorioallantoic membrane assay at 270 nM, and peptide 400-455 was also inhibitory (79%). HK D5 (for which we suggest the designation, "kininostatin") is a potent inhibitor of endothelial cell migration and proliferation in vitro and of angiogenesis in vivo.

ACCESSION NUMBER: 2000:104334 BIOSIS
DOCUMENT NUMBER: PREV200000104334
TITLE: Domain 5 of high molecular weight kininogen (kininostatin) down-regulates endothelial cell proliferation and migration and inhibits angiogenesis.
AUTHOR(S): Colman, Robert W. (1); Jameson, Bradford A.; Lin, Yingzhang; Johnson, Donald; Mousa, Shaker A.
CORPORATE SOURCE: (1) Temple University School of Medicine, 3400 North Broad St, Philadelphia, PA, 19140 USA
SOURCE: Blood, (Jan. 15, 2000) Vol. 95, No. 2, pp. 543-550. ISSN: 0006-4971.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

L5 ANSWER 4 OF 19 USPATFULL
TI DNA fragmentation factor involved in apoptosis
AB The invention provides methods and compositions relating to DNA Fragmentation Factor (DFF) polypeptides and related nucleic acids. More particularly, the present invention provides the sequence for the active subunit of DFF. The polypeptides may be produced recombinantly from host cells transformed from the disclosed DFF encoding nucleic acids or purified from human cells. The invention provides isolated DFF hybridization probes and primers capable of specifically hybridization with the disclosed DFF genes, DFF-specific binding agents such as specific antibodies, and methods of making and using the subject compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2000:174366 USPATFULL
TITLE: DNA fragmentation factor involved in apoptosis
INVENTOR(S): Wang, Xiaodong, Dallas, TX, United States
Liu, Xuesong, Dallas, TX, United States
PATENT ASSIGNEE(S): The University of Texas System Board of Regents, Austin, TX, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6165737		20001226
APPLICATION INFO.:	US 1998-61702		19980416 (9)
DOCUMENT TYPE:	Utility		
PRIMARY EXAMINER:	Achutamurthy, Ponnathapu		
ASSISTANT EXAMINER:	Moore, William W.		
LEGAL REPRESENTATIVE:	Fulbright & Jaworski L.L.P.		
NUMBER OF CLAIMS:	20		

EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 5176
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 5 OF 19 USPATFULL

TI Serine protease inhibitors comprising .alpha.-keto heterocycles
AB Provided are methods of inhibiting the activity of a serine protease using protease inhibitors that include an alpha-keto heterocycle in their structure. The methods are useful in the treatment of ischemic heart or treatment of symptoms associated with blood coagulation disorders. Also provided are methods for detecting or quantifying the activity of a serine protease in a pure sample.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2000:167985 USPATFULL
TITLE: Serine protease inhibitors comprising .alpha.-keto heterocycles
INVENTOR(S): Gyorkos, Albert C., Westminster, CO, United States
Spruce, Lyle W., Arvada, CO, United States
Leimer, Axel H., Lakewood, CO, United States
Cheronis, John C., Conifer, CO, United States
PATENT ASSIGNEE(S): Cortech, Inc., United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6159938		20001212
APPLICATION INFO.:	US 1997-859242		19970520 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1996-761190, filed on 6 Dec 1996, now patented, Pat. No. US 5807829 which is a continuation-in-part of Ser. No. US 1994-345820, filed on 21 Nov 1994, now patented, Pat. No. US 5618792		
DOCUMENT TYPE:	Utility		
PRIMARY EXAMINER:	Russel, Jeffrey E.		
LEGAL REPRESENTATIVE:	Dechert		
NUMBER OF CLAIMS:	77		
EXEMPLARY CLAIM:	1		
LINE COUNT:	1841		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 6 OF 19 USPATFULL

TI Method for assaying for modulators of cytokines of the TFG .beta. superfamily
AB The invention relates to a method for assaying for the presence of a substance that modulates a cytokine of the TGF.beta. superfamily. A substance which is suspected of modulating a cytokine of the TGF.beta. superfamily and a TGF.beta. binding compound which is not a TGF.beta. receptor and which contains a TRH1 domain, or a portion or mimetic thereof, is reacted with a cytokine of the TGF.beta. superfamily under conditions where the compound, portion or mimetic thereof, and the cytokine are capable of forming a complex. Complexes, free compound and/or cytokine are assayed and compared with a control. The invention also relates to a composition comprising at least one compound which is not a TGF.beta. receptor and which contains the TRH1 domain or a portion, or a mimetic thereof, and a pharmaceutically acceptable carrier, auxiliary or excipient and to methods of treatment using the composition. Further the invention relates to a method of enhancing the activity of growth factors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 1998:134826 USPATFULL
TITLE: Method for assaying for modulators of cytokines of the TFG .beta. superfamily

INVENTOR(S): Dennis, James W., Etobicoke, Canada
Demetriou, Michael, Toronto, Canada
PATENT ASSIGNEE(S): Mount Sinai Hospital Corporation, Toronto, Canada
(non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5830671		19981103
APPLICATION INFO.:	US 1997-854768		19970512 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1994-237715, filed on 4 May 1994		
DOCUMENT TYPE:	Utility		
PRIMARY EXAMINER:	Ulm, John		
ASSISTANT EXAMINER:	Mertz, Prema		
LEGAL REPRESENTATIVE:	Merchant, Gould, Smith, Edell, Welter & Schmidt		
NUMBER OF CLAIMS:	13		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	11 Drawing Figure(s); 11 Drawing Page(s)		
LINE COUNT:	1480		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 7 OF 19 USPATFULL

TI Aptamers specific for biomolecules and methods of making
AB A method for identifying oligomer sequences, optionally comprising modified base, which specifically bind target molecules such as serum proteins, kinins, eicosanoids and extracellular proteins is described. The method is used to generate aptamers that bind to serum Factor X, PDGF, FGF, ICAM, VCAM, E-selectin, thrombin, bradykinin, PGF2 and cell surface molecules. The technique involves complexation of the target molecule with a mixture of oligonucleotides containing random sequences and sequences which serve as primer for PCR under conditions wherein a complex is formed with the specifically binding sequences, but not with the other members of the oligonucleotide mixture. The complex is then separated from uncomplexed oligonucleotides and the complexed members of the oligonucleotide mixture are recovered from the separated complex using the polymerase chain reaction. The recovered oligonucleotides may be sequenced, and successive rounds of selection using complexation, separation, amplification and recovery can be employed. The oligonucleotides can be used for therapeutic and diagnostic purposes and for generating secondary aptamers.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 1998:57716 USPATFULL
TITLE: Aptamers specific for biomolecules and methods of making
INVENTOR(S): Griffin, Linda, Atherton, CA, United States
Albrecht, Glenn, Redwood City, CA, United States
Latham, John, Palo Alto, CA, United States
Leung, Lawrence, Hillsborough, CA, United States
Vermaas, Eric, Oakland, CA, United States
Toole, John J., Burlingame, CA, United States
PATENT ASSIGNEE(S): Gilead Sciences, Inc., Foster City, CA, United States
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5756291		19980526
APPLICATION INFO.:	US 1995-484192		19950607 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1992-934387, filed on 21 Aug 1992, now abandoned		
DOCUMENT TYPE:	Utility		

PRIMARY EXAMINER: Zitomer, Stephanie W.
 LEGAL REPRESENTATIVE: Bosse, Mark L.
 NUMBER OF CLAIMS: 12
 EXEMPLARY CLAIM: 1
 NUMBER OF DRAWINGS: 6 Drawing Figure(s); 6 Drawing Page(s)
 LINE COUNT: 8242
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2001 ACS

TI **Inhibition of angiogenesis** by high-molecular-weight
kininogen domain 3 **peptide** analogs

AB **Peptide** analogs the high-mol.-wt. **kininogen** domain 3
 are potent inhibitors of **angiogenesis**. The peptides have the
 formula (a) X1-Asn-Asn-Ala-Thr-Phe-Tyr-Phe-Lys-X2, (b)
 X3-Cys-Val-Gly-Cys-X4, (c) X5-Leu-Asp-X7-Asn-Ala-Glu-Val-Tyr-X6, or (d)
 Tyr-Phe-Ile-Asp-Phe-Val-Ala-Arg-Glu-Thr-Thr-X7-Ser-Lys-Glu-Ser (X1-X6 =
 0-12 amino acids, more preferably 0-6 amino acids; X7 = Ala, Cys). The
 peptides may also comprise biol. active fragments of high-mol.-wt.
kininogen domain 3. Methods of inhibiting endothelial cell
 proliferation and **angiogenesis** are provided.

ACCESSION NUMBER: 2000:420922 HCAPLUS

DOCUMENT NUMBER: 133:68945

TITLE: **Inhibition of angiogenesis** by
 high-molecular-weight **kininogen** domain 3
peptide analogs

INVENTOR(S): McCrae, R. Keith

PATENT ASSIGNEE(S): Temple University - of the Commonwealth System of
 Higher Education, USA

SOURCE: PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035407	A2	20000622	WO 1999-US28465	19991202
WO 2000035407	A3	20000908		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,			
	CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,			
	IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,			
	MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,			
	SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ,			
	BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,			
	DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,			
	CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 2000017494	A1	20000703	AU 2000-17494	19991202
PRIORITY APPLN. INFO.:			US 1998-112427	P 19981216
			WO 1999-US28465	W 19991202

OTHER SOURCE(S): MARPAT 133:68945

L5 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2001 ACS

TI **Inhibition of angiogenesis** and endothelial cell
 proliferation by high-molecular-weight **kininogen** and
peptide analogs thereof

AB Two-chain high-mol.-wt. **kininogen**, and **peptide** analogs
 thereof having homol. to sites within **kininogen** domain 5, are
 potent inhibitors of **angiogenesis**. The peptides have the
 formula X1-His-Lys-X-Lys-X2 (X = any amino acid; X1, X2= 0-12 amino
 acids,
 more preferably 0-6 amino acids, most preferably 0-3 amino acids). X is
 preferably an amino acid having a nonpolar side chain, or a polar side

chain which is uncharged at pH 6.0 to 7.0. X is most preferably Asn, Phe or His. Methods of inhibiting endothelial cell proliferation and **angiogenesis** are provided.

ACCESSION NUMBER: 2000:335430 HCAPLUS
DOCUMENT NUMBER: 133:802
TITLE: **Inhibition of angiogenesis** and endothelial cell proliferation by high-molecular-weight **kininogen** and **peptide** analogs thereof
INVENTOR(S): Mccrae, R. Keith
PATENT ASSIGNEE(S): Temple University - of the Commonwealth System of Higher Education, USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027866	A1	20000518	WO 1999-US26419	19991105
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 1998-107833	P 19981110
OTHER SOURCE(S):			MARPAT 133:802	
REFERENCE COUNT:			10	
REFERENCE(S):			(1) Dennis; US 5830671 A 1998 HCAPLUS (2) Griffin; US 5756291 A 1998 HCAPLUS (3) Guerinot; US 5846821 A 1998 HCAPLUS (4) Heitsch; US 5786365 A 1998 HCAPLUS (7) Lottspeich; European Journal of Biochemistry	

1985,

V152, P307 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2001 ACS
TI **Inhibition of angiogenesis** by **peptide** analogs of high-molecular-weight **kininogen** domain 5
AB A method for **inhibition** of endothelial cell proliferation in a mammal comprises peptides and proteins of high-mol.-wt. **kininogen** light chain (domain 5). For example, glutathione-S-transferase (GST) fusion proteins with high-mol.-wt. **kininogen** light chain peptides, i.e. Lys(420)-Ser(513) (SEQ ID NO: 10) and His(441)-Ser(626) (SEQ ID NO: 8), at concns. of 0.27 and 0.39 .mu.M, resp. induced 100% **inhibition** of proliferation of human umbilical vein endothelial cells (HUVEC). Also, GST-SEQ ID NO: 10 at a concn. of 0.27 .mu.M achieved

100% **inhibition** of HUVEC migration to vitronectin.
ACCESSION NUMBER: 2000:335256 HCAPLUS
DOCUMENT NUMBER: 132:343359
TITLE: **Inhibition of angiogenesis** by **peptide** analogs of high-molecular-weight **kininogen** domain 5
INVENTOR(S): Colman, W. Robert; Mousa, A. Shaker
PATENT ASSIGNEE(S): Temple University - of the Commonwealth System of Higher Education, USA; Dupont Pharmaceuticals Company

SOURCE: PCT Int. Appl., 41 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027415	A2	20000518	WO 1999-US26377	19991109
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1044012	A1	20001018	EP 1999-957529	19991109
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRIORITY APPLN. INFO.:			US 1998-107844	P 19981110
			WO 1999-US26377	W 19991109

L5 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2001 ACS
 TI Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and inhibits **angiogenesis**
 AB We have demonstrated that high mol. wt. **kininogen** (HK) binds specifically on endothelial cells to domain 2/3 of the urokinase receptor (uPAR). **Inhibition** by vitronectin suggests that kallikrein-cleaved HK (HKa) is antiadhesive. Plasma kallikrein bound to HK cleaves prourokinase to urokinase, initiating cell-assocd. fibrinolysis. We postulated that HK cell binding domains would inhibit **angiogenesis**. We found that recombinant domain 5 (D5) inhibited endothelial cell migration toward vitronectin 85% at 0.27 .mu.M with an IC50 (concn. to yield 50% **inhibition**) = 0.12 .mu.M. A D5 **peptide**, G486-K502, showed an IC50 = 0.2 .mu.M, but a 25-mer **peptide** from a D3 cell binding domain only inhibited migration 10% at 139 .mu.M (IC50 > 50 .mu.M). D6 exhibited weaker inhibitory activity (IC50 = 0.50 .mu.M). D5 also potentially inhibited endothelial cell proliferation with an IC50 = 30 nM, while D3 and D6 were inactive. Using deletion mutants of D5, we localized the smallest region for full activity to H441-D474. To further map the active region, we created a mol. homol. model of D5 and designed a series of peptides displaying surface loops. **Peptide** 440-455 was the most potent (IC50 = 100 nM) in inhibiting proliferation but did not inhibit migration. D5 inhibited **angiogenesis** stimulated by fibroblast growth factor FGF2 (97%) in a chicken chorioallantoic membrane assay at 270 nM, and **peptide** 400-455 was also inhibitory (79%). HK D5 (for which we suggest the designation, "kininostatin") is a potent inhibitor of endothelial cell migration and proliferation in vitro and of **angiogenesis** in vivo.

ACCESSION NUMBER: 2000:55516 HCAPLUS
 DOCUMENT NUMBER: 132:164060
 TITLE: Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and inhibits **angiogenesis**
 AUTHOR(S): Colman, Robert W.; Jameson, Bradford A.; Lin, Yingzhang; Johnson, Donald; Mousa, Shaker A.
 CORPORATE SOURCE: Sol Sherry Thrombosis Research Center, Temple

SOURCE: University School of Medicine, Philadelphia, PA, USA
 Blood (2000), 95(2), 543-550
 CODEN: BLOOAW; ISSN: 0006-4971
 PUBLISHER: American Society of Hematology
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 REFERENCE COUNT: 52
 REFERENCE(S): (1) Asakura, S; J Cell Biol 1992, V116, P465 HCAPLUS
 (3) Bacharach, E; Proc Natl Acad Sci U S A 1992, V89, P10686 HCAPLUS
 (4) Barnathan, E; Blood 1990, V76, P1795 HCAPLUS
 (5) Behrendt, N; J Biol Chem 1991, V266, P7842
 HCAPLUS
 (7) Bradford, H; Blood 1997, V90, P1508 HCAPLUS
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 19 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 TI Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
 AB The present sequence is that of a D3 **peptide** derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 **peptide** inhibits endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3, in this case Tyr299-Ser314, and in which native cysteine residues may be replaced by alanine residues. The peptides inhibit endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for inhibiting **angiogenesis**, inhibiting endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated. The IC50 value for the present **peptide** was 28 uM for inhibition of fibroblast growth factor-induced HUVEC cell proliferation.
 ACCESSION NUMBER: AAY95423 Peptide DGENE
 TITLE: Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
 INVENTOR: McCrae R K
 PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
 (MCCR-I) MCCRAE R K.
 PATENT INFO: WO 2000035407 A2 20000622 44p
 APPLICATION INFO: WO 1999-US28465 19991202
 PRIORITY INFO: US 1998-112427 19981216
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 2000-442247 [38]

L5 ANSWER 13 OF 19 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 TI Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
 AB The present sequence is that of a D3 **peptide** derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 **peptide** inhibits endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in

the HK domain 3, in this case amino acid residues Leu331-Tyr338, and in which native cysteine residues may be replaced by alanine residues. The peptides inhibit endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used

in claimed methods for inhibiting **angiogenesis**, inhibiting endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated. The IC50 value for the present **peptide** was 44 uM for **inhibition** of fibroblast growth factor-induced HUVEC cell proliferation.

ACCESSION NUMBER: AAY95421 Peptide DGENE

TITLE: Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -

INVENTOR: McCrae R K

PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.

PATENT INFO: WO 2000035407 A2 20000622

44p

APPLICATION INFO: WO 1999-US28465 19991202

PRIORITY INFO: US 1998-112427 19981216

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2000-442247 [38]

L5 ANSWER 14 OF 19 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

TI Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -

AB The present sequence is that of a D3 **peptide** derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 **peptide** inhibits endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3, in this case amino acid residues Leu331-Tyr338, and in which native cysteine residues may be replaced by alanine residues. The peptides inhibit endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are

used

in claimed methods for inhibiting **angiogenesis**, inhibiting endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated. The IC50 value for the present **peptide** was 42 uM for **inhibition** of fibroblast growth factor-induced HUVEC cell proliferation.

ACCESSION NUMBER: AAY95420 Peptide DGENE

TITLE: Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -

INVENTOR: McCrae R K

PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.

PATENT INFO: WO 2000035407 A2 20000622

44p

APPLICATION INFO: WO 1999-US28465 19991202

PRIORITY INFO: US 1998-112427 19981216

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2000-442247 [38]

L5 ANSWER 15 OF 19 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a D3 **peptide** derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 **peptide** inhibits endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3, in this case amino acid residues Cys246-Cys249. The peptides inhibit endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are

used in claimed methods for inhibiting **angiogenesis**, inhibiting endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated. The IC50 value for the present **peptide** was 30 uM for inhibition of fibroblast growth factor-induced HUVEC cell proliferation.

ACCESSION NUMBER: AAY95415 Peptide DGENE
TITLE: Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L5 ANSWER 16 OF 19 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a D3 **peptide** derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 **peptide** inhibits endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3, in this case amino acid residues Asn275-Lys282. The peptides inhibit endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are

used in claimed methods for inhibiting **angiogenesis**, inhibiting endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated. The IC50 value for the present **peptide** was less than 0.8 uM for inhibition of fibroblast growth factor-induced HUVEC cell proliferation.

ACCESSION NUMBER: AAY95410 Peptide DGENE
TITLE: Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.

(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622
APPLICATION INFO: WO 99-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

44p

L5 ANSWER 17 OF 19 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a D3 **peptide** derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 **peptide** inhibits endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3, in this case amino acid residues Asn275-Lys282. The peptides inhibit endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for inhibiting **angiogenesis**, inhibiting endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated. The IC50 value for the present **peptide** was less than 0.8 uM for inhibition of fibroblast growth factor-induced HUVEC cell proliferation.

ACCESSION NUMBER: AAY95409 Peptide DGENE
TITLE: Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

44p

L5 ANSWER 18 OF 19 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
TI Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and inhibits **angiogenesis**.
AB We have demonstrated that high molecular weight **kininogen** (HK) binds specifically on endothelial cells to domain 2/3 of the urokinase receptor (uPAR). **Inhibition** by vitronectin suggests that kallikrein-cleaved HK (HKa) is antiadhesive. Plasma kallikrein bound to HK cleaves prourokinase to urokinase, initiating cell-associated fibrinolysis. We postulated that HK cell binding domains would inhibit **angiogenesis**. We found that recombinant domain 5 (D5) inhibited endothelial cell migration toward vitronectin 85% at 0.27 .mu.M with an IC50 (concentration to yield 50% **inhibition**) = 0.12 .mu.M. A D5 **peptide**, G486-K502, showed an IC50 = 0.2 .mu.M, but a 25-mer **peptide** from a D3 cell binding domain only inhibited migration 10% at 139 .mu.M (IC50 > 50 .mu.M). D6 exhibited weaker inhibitory activity (IC50 = 0.50 .mu.M). D5 also potently inhibited endothelial cell proliferation with an IC50 = 30 nM, while D3 and D6 were inactive. Using deletion mutants of D5, we localized the smallest region for full activity

to H441-D474. To further map the active region, we created a molecular homology model of D5 and designed a series of peptides displaying surface loops. **Peptide** 400-455 was the most potent (IC₅₀ = 100 nM) in inhibiting proliferation but did not inhibit migration. D5 inhibited **angiogenesis** stimulated by fibroblast growth factor FGF2 (97%) in a chicken chorioallantoic membrane assay at 270 nM, and **peptide** 400-455 was also inhibitory (79%). HK D5 (for which we suggest the designation, 'kininostatin') is a potent inhibitor of endothelial cell migration and proliferation in vitro and of **angiogenesis** in vivo.

ACCESSION NUMBER: 2000028682 EMBASE
 TITLE: Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and inhibits **angiogenesis**.
 AUTHOR: Colman R.W.; Jameson B.A.; Lin Y.; Johnson D.; Mousa S.A.
 CORPORATE SOURCE: R.W. Colman, Sol Sherry Thrombosis Res. Center, Temple University School of Medicine, 3400 North Broad St, Philadelphia, PA 19140, United States. colmanr@astro.temple.edu
 SOURCE: Blood, (15 Jan 2000) 95/2 (543-550). Refs: 52
 ISSN: 0006-4971 CODEN: BLOOAW
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 025 Hematology
 029 Clinical Biochemistry
 LANGUAGE: English
 SUMMARY LANGUAGE: English

L5 ANSWER 19 OF 19 SCISEARCH COPYRIGHT 2001 ISI (R)
 TI Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and inhibits **angiogenesis**

AB We have demonstrated that high molecular weight **kininogen** (HK) binds specifically on endothelial cells to domain 2/3 of the urokinase receptor (uPAR). **Inhibition** by vitronectin suggests that kallikrein-cleaved HK (HKa) is antiadhesive. Plasma kallikrein bound to HK cleaves prourokinase to urokinase, initiating cell-associated fibrinolysis. We postulated that HK cell binding domains would inhibit **angiogenesis**. We found that recombinant domain 5 (D5) inhibited endothelial cell migration toward vitronectin 85% at 0.27 μ M with an IC₅₀ (concentration to yield 50% **inhibition**) = 0.12 μ M. A D5 **peptide**, G486-K502, showed an IC₅₀ = 0.2 μ M, but a 25-mer **peptide** from a D3 cell binding domain only inhibited migration 10% at 139 μ M (IC₅₀ > 50 μ M). D6 exhibited weaker inhibitory activity (IC₅₀ = 0.50 μ M). D5 also potentially inhibited endothelial cell proliferation with an IC₅₀ = 30 nM, while D3 and D6 were inactive. Using deletion mutants of D5, we localized the smallest region for full activity

to H441-D474. To further map the active region, we created a molecular homology model of D5 and designed a series of peptides displaying surface loops. **Peptide** 440-155 was the most potent (IC₅₀ = 100 nM) in inhibiting proliferation but did not inhibit migration. D5 inhibited **angiogenesis** stimulated by fibroblast growth factor FGF2 (97%) in a chicken chorioallantoic membrane assay at 270 nM, and **peptide** 400-455 was also inhibitory (79%), HK D5 (for which we suggest the designation, 'kininostatin') is a potent inhibitor of endothelial cell migration and proliferation in vitro and of **angiogenesis** in vivo. (Blood, 2000;95:543-550) (C) 2000 by The American Society of Hematology.

ACCESSION NUMBER: 2000:48248 SCISEARCH
 THE GENUINE ARTICLE: 272QG
 TITLE: Domain 5 of high molecular weight **kininogen**

(kininostatin) down-regulates endothelial cell proliferation and migration and inhibits angiogenesis

AUTHOR: Colman R W (Reprint); Jameson B A; Lin Y Z; Johnson D; Mousa S A

CORPORATE SOURCE: TEMPLE UNIV, SOL SHERRY THROMBOSIS RES CTR, SCH MED, 3400 N BROAD ST, PHILADELPHIA, PA 19140 (Reprint); MCP HAHNEMANN MED SCH, CTR NEUROVIROL, PHILADELPHIA, PA; DUPONT MERCK PHARMACEUT CO, DIV CARDIOVASC, WILMINGTON, DE 19880

COUNTRY OF AUTHOR: USA

SOURCE: BLOOD, (15 JAN 2000) Vol. 95, No. 2, pp. 543-550. Publisher: AMER SOC HEMATOLOGY, 1200 19TH ST, NW, STE 300, WASHINGTON, DC 20036-2422. ISSN: 0006-4971.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE; CLIN

LANGUAGE: English

REFERENCE COUNT: 51

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

=> d his

(FILE 'HOME' ENTERED AT 13:14:38 ON 13 JUL 2001)

FILE 'MEDLINE, BIOSIS, USPATFULL, HCAPLUS, DGENE, EMBASE, SCISEARCH, WPIDS, JAPIO, JICST-EPLUS, FSTA, FROSTI, CEN, CEABA-VTB, CABA' ENTERED

AT

13:15:24 ON 13 JUL 2001

L1 111516 S ANGIOGENESIS
L2 20392 S L1 AND INHIBITION
L3 6317 S L2 AND PEPTIDE
L4 10807 S KININOGEN
L5 19 S L3 AND L4

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E2 2 MCCRAE WM/AU
E3 0 --> MCCRAE, K/AU
E4 1 MCCRAEHOMSMA C H/AU
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E10 1 MCCRAIG J/AU
E11 1 MCCRAIG J OSCAR/AU
E12 1 MCCRAIG L F/AU

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E1 1 COLMAN WM P/AU
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E3 0 --> COLMAN,R/AU
E4 2 COLMANDEJEAN T/AU
E5 1 COLMANET G/AU
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FILE 'MEDLINE, BIOSIS, USPATFULL, HCAPLUS, DGENE, EMBASE, SCISEARCH,
WPIDS, JAPIO, JICST-EPLUS, FSTA, FROSTI, CEN, CEABA-VTB, CABA' ENTERED
AT
13:15:24 ON 13 JUL 2001
L1      111516 S ANGIOGENESIS
L2      20392 S L1 AND INHIBITION
L3      6317 S L2 AND PEPTIDE
L4      10807 S KININOGEN
L5      19 S L3 AND L4
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          E COLMAN, R/AU

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MISSING OPERATOR L4 ANS

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L6      107 L4 AND L1

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=> s l6 and inhibit?

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13 FILES SEARCHED...
L7      95 L6 AND INHIBIT?

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L7      ANSWER 1 OF 95  MEDLINE
TI      Two-chain high molecular weight kininogen induces endothelial
        cell apoptosis and inhibits angiogenesis: partial
        activity within domain 5.
AB      We previously reported that the binding of two-chain high molecular
weight
kininogen (HKa) to endothelial cells may occur through
interactions with endothelial urokinase receptors. Since the binding of
urokinase to urokinase receptors activates signaling responses and may
stimulate mitogenesis, we assessed the effect of HKa binding on
endothelial cell proliferation. Unexpectedly, HKa inhibited
proliferation in response to several growth factors, with 50%
inhibition caused by approximately 10 nM HKa. This activity was
Zn(2+) dependent and not shared by either single-chain high molecular
weight kininogen (HK) or low molecular weight kininogen
. HKa selectively inhibited the proliferation of human umbilical
vein and dermal microvascular endothelial cells, but did not affect that
of umbilical vein or human aortic smooth muscle cells, trophoblasts,
fibroblasts, or carcinoma cells. Inhibition of endothelial
proliferation by HKa was associated with endothelial cell apoptosis and
unaffected by antibodies that block the binding of HK or HKa to any of
their known endothelial receptors. Recombinant HK domain 5 displayed
activity similar to that of HKa. In vivo, HKa inhibited
neovascularization of subcutaneously implanted Matrigel plugs, as well as

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rat corneal **angiogenesis**. These results demonstrate that HKa is a novel **inhibitor of angiogenesis**, whose activity is dependent on the unique conformation of the two-chain molecule.

ACCESSION NUMBER: 2001111838 MEDLINE
DOCUMENT NUMBER: 20553282 PubMed ID: 11099478
TITLE: Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits angiogenesis**: partial activity within domain 5.

AUTHOR: Zhang J C; Claffey K; Sakthivel R; Darzynkiewicz Z; Shaw D E; Leal J; Wang Y C; Lu F M; McCrae K R
CORPORATE SOURCE: Hematology-Oncology Division, Case Western Reserve University, School of Medicine, Cleveland, Ohio 44106-4937, USA.

CONTRACT NUMBER: CA83134 (NCI)
HL50827 (NHLBI)

SOURCE: FASEB JOURNAL, (2000 Dec) 14 (15) 2589-600.
Journal code: FAS. ISSN: 0892-6638.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered PubMed: 20010205
Entered Medline: 20010208

L7 ANSWER 2 OF 95 MEDLINE

TI Local delivery of human tissue kallikrein gene accelerates spontaneous **angiogenesis** in mouse model of hindlimb ischemia.

AB BACKGROUND: Human tissue kallikrein (HK) releases kinins from **kininogen**. We investigated whether adenovirus-mediated HK gene delivery is angiogenic in the context of ischemia. METHODS AND RESULTS: Hindlimb ischemia, caused by femoral artery excision, increased muscular capillary density (P:<0.001) and induced the expression of kinin B(1) receptor gene (P:<0.05). Pharmacological blockade of B(1) receptors blunted ischemia-induced **angiogenesis** (P:<0.01), whereas kinin B(2) receptor antagonism was ineffective. Intramuscular delivery of adenovirus containing the HK gene (Ad. CMV-CHK) enhanced the increase in capillary density caused by ischemia (969+/-32 versus 541+/-18 capillaries/mm(2) for control, P:<0.001), accelerated blood flow recovery (P:<0.01), and preserved energetic charge of ischemic muscle (P:<0.01). Chronic blockade of kinin B(1) or B(2) receptors prevented HK-induced **angiogenesis**. CONCLUSIONS: HK gene delivery enhances the native angiogenic response to ischemia. **Angiogenesis** gene therapy with HK might be applicable to peripheral occlusive vascular disease.

ACCESSION NUMBER: 2001087991 MEDLINE
DOCUMENT NUMBER: 20579827 PubMed ID: 11136697
TITLE: Local delivery of human tissue kallikrein gene accelerates spontaneous **angiogenesis** in mouse model of hindlimb ischemia.

AUTHOR: Emanuelli C; Minasi A; Zacheo A; Chao J; Chao L; Salis M B; Straino S; Tozzi M G; Smith R; Gaspa L; Bianchini G; Stillo F; Capogrossi M C; Madeddu P
CORPORATE SOURCE: Laboratorio di Patologia Vascolare, Istituto Dermopatico dell'Immacolata, Rome, Italy.

CONTRACT NUMBER: HL-29397 (NHLBI)
HL-52196 (NHLBI)

SOURCE: CIRCULATION, (2001 Jan 2) 103 (1) 125-32.
Journal code: DAW; 0147763. ISSN: 1524-4539.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 2001
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010521
Entered PubMed: 20010109
Entered Medline: 20010118

L7 ANSWER 3 OF 95 MEDLINE

TI Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and **inhibits angiogenesis**.

AB We have demonstrated that high molecular weight **kininogen** (HK) binds specifically on endothelial cells to domain 2/3 of the urokinase receptor (uPAR). **Inhibition** by vitronectin suggests that kallikrein-cleaved HK (HKa) is antiadhesive. Plasma kallikrein bound to

HK cleaves prourokinase to urokinase, initiating cell-associated fibrinolysis. We postulated that HK cell binding domains would **inhibit angiogenesis**. We found that recombinant domain 5 (D5) **inhibited** endothelial cell migration toward vitronectin 85% at 0.27 microM with an IC(50) (concentration to yield 50% **inhibition**) = 0.12 microM. A D5 peptide, G486-K502, showed an IC(50) = 0.2 microM, but a 25-mer peptide from a D3 cell binding domain only **inhibited** migration 10% at 139 microM (IC(50) > 50 microM). D6 exhibited weaker **inhibitory** activity (IC(50) = 0.50 microM). D5 also potentially **inhibited** endothelial cell proliferation with an IC(50) = 30 nM, while D3 and D6 were inactive. Using deletion mutants of D5, we localized the smallest region for full activity to H441-D474.

To further map the active region, we created a molecular homology model of
D5

and designed a series of peptides displaying surface loops. Peptide 440-455 was the most potent (IC(50) = 100 nM) in **inhibiting** proliferation but did not **inhibit** migration. D5 **inhibited angiogenesis** stimulated by fibroblast growth factor FGF2 (97%) in a chicken chorioallantoic membrane assay at 270 nM, and peptide 400-455 was also **inhibitory** (79%). HK D5 (for which we suggest the designation, "kininostatin") is a potent **inhibitor** of endothelial cell migration and proliferation in vitro and of **angiogenesis** in vivo. (Blood. 2000;95:543-550)

ACCESSION NUMBER: 2000094677 MEDLINE

DOCUMENT NUMBER: 20094677 PubMed ID: 10627460

TITLE: Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and **inhibits angiogenesis**.

AUTHOR: Colman R W; Jameson B A; Lin Y; Johnson D; Mousa S A

CORPORATE SOURCE: Sol Sherry Thrombosis Research Center, Temple University School of Medicine, Philadelphia, PA 19140, USA..
colmanr@astro.temple.edu

CONTRACT NUMBER: P01HL56914 (NHLBI)
R01CA63938 (NCI)

SOURCE: BLOOD, (2000 Jan 15) 95 (2) 543-50.

Journal code: A8G; 7603509. ISSN: 0006-4971.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200002

ENTRY DATE: Entered STN: 20000209

Last Updated on STN: 20000209

Entered Medline: 20000203

L7 ANSWER 4 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS
 TI Peptides derived from high molecular weight **kininogen** (HK) domains 3 and 5 **inhibit** endothelial cell proliferation and induce endothelial cell apoptosis.
 AB We have recently reported that two-chain high molecular weight **kininogen** (HKa) **inhibits** endothelial cell proliferation, induces endothelial cell apoptosis and **inhibits angiogenesis**. Recombinant high molecular weight **kininogen** domain 5 expresses similar activity, **inhibiting** endothelial cell proliferation by 50% (IC50) at a concentration of approx 60 nM. To further define the regions within **kininogen** domain 5 responsible for these effects, we prepared overlapping 16 amino acid peptides (each overlapping by 8 amino acids) encompassing **kininogen** domain 5 (aa 384-509), and measured their ability to **inhibit** endothelial cell proliferation and induce endothelial cell apoptosis. A similar strategy was used to assess potentially active regions within HK domain 3,

which also contains regions that mediate binding of HK to endothelial cells. The most potent domain 5-derived peptides were found in the C-terminal region of the domain. H5-13 (KHGHGHGKHKNKGKKN; aa 480-495 of HK) **inhibited** endothelial cell proliferation by 86 +/- 13% at a concentration of 50 μ M (IC50 approx 8 μ M), while H5-14 (HKNKGKKNKGKHNGWKT; aa 488-503 of HK), used at the same concentration, **inhibited** proliferation by 93 +/- 7% (IC50 approx 14 μ M). As observed with HKa and recombinant domain 5, the peptides caused endothelial cell apoptosis, and their activity was enhanced in the presence of Zn²⁺. These results differ from a previous report, in which the domain 5 peptide most active in **inhibiting** endothelial cell proliferation was found to encompass amino acids 440-455 of HK. In addition, we also observed that two 16 amino acid peptides from HK domain 3 (H3-6, aa 267-282 of HK; H3-7, aa 275-290 of HK) also **inhibited** endothelial cell proliferation (IC50 approx 1 μ M) and induced apoptosis, though they were not freely soluble in aqueous buffers. Exogenous Zn²⁺ did not significantly affect the activity of the latter peptides. Neither the domain 3 or domain 5 peptides affected the proliferation of a number of other cell types, including primary cultures of fibroblasts and smooth muscle cells. These studies define active regions within HK domains 3 and 5 that **inhibit** endothelial cell proliferation and induce endothelial cell apoptosis. Current studies are focused on evaluating the antiangiogenic activity of these peptides in vitro.

ACCESSION NUMBER: 2001:312300 BIOSIS
 DOCUMENT NUMBER: PREV200100312300
 TITLE: Peptides derived from high molecular weight **kininogen** (HK) domains 3 and 5 **inhibit** endothelial cell proliferation and induce endothelial cell apoptosis.
 AUTHOR(S): Zhang, Jing-Chuan (1); Juarez, Jose; Shaw, David Elliott; Mazar, Andrew P.; McCrae, Keith R. (1)
 CORPORATE SOURCE: (1) Hematology-Oncology, Case Western Reserve University School of Medicine, Cleveland, OH USA
 SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 41a.
 print.
 Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
 . ISSN: 0006-4971.
 DOCUMENT TYPE: Conference
 LANGUAGE: English
 SUMMARY LANGUAGE: English

L7 ANSWER 5 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS
TI Kininostatin induces apoptosis of endothelial cells.
AB Kininostatin (D5 domain 5 of high molecular weight kininogen (HK), is a recently discovered angiogenic inhibitor. Previously we reported that D5 inhibited two important steps required for angiogenesis: proliferation and migration of endothelial cells. Anti-angiogenic activity was further demonstrated in an in vivo model by studying neovascularization in the CAM (Chicken chorioAllantoic Membrane).

D5 inhibited new blood vessel formation 85% compared to that stimulated by bFGF in CAM. We proposed that D5 may function as a naturally occurring angiogenesis inhibitor because it is proteolytically cleaved from HK, a multifunctional plasma protein that plays important roles in adhesion, fibrinolysis and inflammation. To understand the mechanism of the antiangiogenic effect of D5, we investigated whether the inhibition of endothelial cell proliferation is associated with induction of apoptosis. We found that human umbilical vein endothelial cells (HUVEC) undergo rapid apoptosis when cultured in a serum-free medium, and this alteration can be prevented

by addition of 10 ng/ml bFGF. Recombinant D5 (200 nM) attenuated the protective effect of bFGF by 80%. The cells treated with D5 in the presence of bFGF showed typical morphological features of apoptosis, such as membrane blebbing and shrinkage of the cell body. The apoptotic cell death was further confirmed by two additional assays: Hoechst 33258 cell staining and DNA fragmentation analysis. D5-treated cells in the presence of bFGF showed an increased number of apoptotic nuclei and an increased amount of fragmented DNA. An interesting finding of this study is that the

number of apoptotic cells was significantly higher among the proliferating cells than among quiescent cells as determined by a microscopic analysis simultaneously detecting mitotic and apoptotic cells. We conclude that D5-induced apoptosis, particularly among proliferating endothelial cells, makes an important contribution to its anti-angiogenic activity.

ACCESSION NUMBER: 2001:264349 BIOSIS
DOCUMENT NUMBER: PREV200100264349
TITLE: Kininostatin induces apoptosis of endothelial cells.
AUTHOR(S): Colman, Robert W. (1); Wang, Shujie (1); Guo, Yan-Lin (1)
CORPORATE SOURCE: (1) Thrombosis Res. Ctr., Temple Univ. Sch. of Med., 3400 N. Broad Street, Philadelphia, PA, 19140 USA
SOURCE: FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A459. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L7 ANSWER 6 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS
TI Role of the light chain of high molecular weight kininogen in adhesion, cell-associated proteolysis and angiogenesis.
AB Cleavage of high molecular weight kininogen (HK) by plasma kallikrein results in a light chain and a heavy chain (HK). The light chain has two domains: D6, which binds (pre)kallikrein, and D5, which binds to anionic surfaces, including heparin as well as zinc. Initially, HK was thought to be important for surface-activated coagulation. HKa or D5 binds to the urokinase receptor on endothelial cells, thereby enhancing the conversion of prourokinase to urokinase by kallikrein, and, thus, cell-associated fibrinolysis. HKa or D5 is antiadhesive by competing with

vitronectin binding to the urokinase receptor and/or forming a complex with vitronectin. D5 **inhibits** endothelial cell migration, proliferation, tube formation and **angiogenesis**, thus modulating inflammation and neovascularization.

ACCESSION NUMBER: 2001:207350 BIOSIS
DOCUMENT NUMBER: PREV200100207350
TITLE: Role of the light chain of high molecular weight **kininogen** in adhesion, cell-associated proteolysis and **angiogenesis**.
AUTHOR(S): Colman, Robert W. (1)
CORPORATE SOURCE: (1) Sol Sherry Thrombosis Research Center, Temple University School of Medicine, Philadelphia, PA, 19140 USA
SOURCE: Biological Chemistry, (January, 2001) Vol. 382, No. 1, pp. 65-70. print.
ISSN: 1431-6730.
DOCUMENT TYPE: General Review
LANGUAGE: English
SUMMARY LANGUAGE: English

L7 ANSWER 7 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS

TI Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits angiogenesis**: Partial activity within domain 5.

AB We previously reported that the binding of two-chain high molecular weight

kininogen (HKa) to endothelial cells may occur through interactions with endothelial urokinase receptors. Since the binding of urokinase to urokinase receptors activates signaling responses and may stimulate mitogenesis, we assessed the effect of HKa binding on endothelial cell proliferation. Unexpectedly, HKa **inhibited** proliferation in response to several growth factors, with 50% **inhibition** caused by approx 10 nM HKa. This activity was Zn²⁺ dependent and not shared by either single-chain high molecular weight **kininogen** (HK) or low molecular weight **kininogen**. HKa selectively **inhibited** the proliferation of human umbilical vein and dermal microvascular endothelial cells, but did not affect that of umbilical vein or human aortic smooth muscle cells, trophoblasts, fibroblasts, or carcinoma cells. **Inhibition** of endothelial proliferation by HKa was associated with endothelial cell apoptosis and unaffected by antibodies that block the binding of HK or HKa to any of their known endothelial receptors. Recombinant HK domain 5 displayed activity similar to that of HKa. In vivo, HKa **inhibited** neovascularization of subcutaneously implanted Matrigel plugs, as well as rat corneal **angiogenesis**. These results demonstrate that HKa is a novel **inhibitor** of angiogenesis, whose activity is dependent on the unique conformation of the two-chain molecule.

ACCESSION NUMBER: 2001:58828 BIOSIS
DOCUMENT NUMBER: PREV200100058828
TITLE: Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits angiogenesis**: Partial activity within domain 5.
AUTHOR(S): Zhang, Jing-Chuan; Claffey, Kevin; Sakthivel, Ramasamy; Darzynkiewicz, Zbigniew; Shaw, David Elliot; Leal, Juan; Wang, Yi-Chun; Lu, Feng-Min; McCrae, Keith R. (1)
CORPORATE SOURCE: (1) Hematology-Oncology Division, Case Western Reserve University, School of Medicine, 10900 Euclid Ave., BRB 3, Cleveland, OH, 44106-4937: kxm71@pocwru.edu USA
SOURCE: FASEB Journal, (December, 2000) Vol. 14, No. 15, pp. 2589-2600. print.
ISSN: 0892-6638.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

L7 ANSWER 8 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS

TI **Inhibition of angiogenesis** by peptides derived from **kininogen** domain 5 and by a monoclonal antibody to **kininogen** domain 5.

ACCESSION NUMBER: 2000:368311 BIOSIS

DOCUMENT NUMBER: PREV200000368311

TITLE: **Inhibition of angiogenesis** by peptides derived from **kininogen** domain 5 and by a monoclonal antibody to **kininogen** domain 5.

AUTHOR(S): Mousa, S. A. (1); Mohamed, S.; Powell, J.; Colman, R. W.

CORPORATE SOURCE: (1) DuPont Pharmaceuticals, Wilmington, DE USA

SOURCE: Fibrinolysis & Proteolysis, (June, 2000) Vol. 14, No. Supplement 1, pp. 39. print.
Meeting Info.: XVth International Congress on Fibrinolysis and Proteolysis Hamamatsu, Japan June 25-29, 2000
ISSN: 1369-0191.

DOCUMENT TYPE: Conference

LANGUAGE: English

SUMMARY LANGUAGE: English

L7 ANSWER 9 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS

TI **Inhibition of angiogenesis** by peptides derived from **kininogen** domain 5 & by a monoclonal antibody to **kininogen** domain 5.

ACCESSION NUMBER: 2000:176604 BIOSIS

DOCUMENT NUMBER: PREV200000176604

TITLE: **Inhibition of angiogenesis** by peptides derived from **kininogen** domain 5 & by a monoclonal antibody to **kininogen** domain 5.

AUTHOR(S): Mousa, Shaker A. (1); Mohamed, Seema; Powell, John; Colman,

Robert W.

CORPORATE SOURCE: (1) DuPont Pharmaceuticals, Wilmington, DE USA

SOURCE: Journal of the American College of Cardiology., (Feb., 2000) Vol. 35, No. 2 suppl. A, pp. 295A-296A.
Meeting Info.: 29th Annual Scientific Session of the American College of Cardiology. Anaheim, California, USA
March 12-15, 2000
ISSN: 0735-1097.

DOCUMENT TYPE: Conference

LANGUAGE: English

SUMMARY LANGUAGE: English

L7 ANSWER 10 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS

TI Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and **inhibits angiogenesis**.

AB We have demonstrated that high molecular weight **kininogen** (HK) binds specifically on endothelial cells to domain 2/3 of the urokinase receptor (uPAR). **Inhibition** by vitronectin suggests that kallikrein-cleaved HK (HKa) is antiadhesive. Plasma kallikrein bound to

HK cleaves prourokinase to urokinase, initiating cell-associated fibrinolysis. We postulated that HK cell binding domains would **inhibit angiogenesis**. We found that recombinant domain 5 (D5) **inhibited** endothelial cell migration toward vitronectin 85% at 0.27 μ M with an IC₅₀ (concentration to yield 50% **inhibition**) = 0.12 μ M. A D5 peptide, G486-K502, showed an IC₅₀ = 0.2 μ M, but a 25-mer peptide from a D3 cell binding domain only **inhibited** migration 10% at 139 μ M (IC₅₀ > 50 μ M). D6 exhibited weaker **inhibitory** activity (IC₅₀ = 0.50 μ M). D5 also potently **inhibited** endothelial cell proliferation with an IC₅₀ = 30 nM, while D3 and D6 were inactive. Using deletion mutants of D5, we localized the smallest region for full activity to H441-D474. To further map the

active region, we created a molecular homology model of D5 and designed a series of peptides displaying surface loops. Peptide 440-455 was the most potent (IC50 = 1 nM) in **inhibiting** proliferation but did not **inhibit** migration. D5 **inhibited angiogenesis** stimulated by fibroblast growth factor FGF2 (97%) in a chicken chorioallantoic membrane assay at 270 nM, and peptide 400-455 was also **inhibitory** (79%). HK D5 (for which we suggest the designation, "kininostatin") is a potent **inhibitor** of endothelial cell migration and proliferation in vitro and of **angiogenesis** in vivo.

ACCESSION NUMBER: 2000:104334 BIOSIS
DOCUMENT NUMBER: PREV200000104334
TITLE: Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and **inhibits angiogenesis**.
AUTHOR(S): Colman, Robert W. (1); Jameson, Bradford A.; Lin, Yingzhang; Johnson, Donald; Mousa, Shaker A.
CORPORATE SOURCE: (1) Temple University School of Medicine, 3400 North Broad St, Philadelphia, PA, 19140 USA
SOURCE: Blood, (Jan. 15, 2000) Vol. 95, No. 2, pp. 543-550. ISSN: 0006-4971.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

L7 ANSWER 11 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS
TI Biologic activities of the contact factors in vivo: Potentiation of hypotension, inflammation, and fibrinolysis, and **inhibition** of cell adhesion, **angiogenesis** and thrombosis.

ACCESSION NUMBER: 2000:87674 BIOSIS
DOCUMENT NUMBER: PREV200000087674
TITLE: Biologic activities of the contact factors in vivo: Potentiation of hypotension, inflammation, and fibrinolysis, and **inhibition** of cell adhesion, **angiogenesis** and thrombosis.
AUTHOR(S): Colman, Robert W. (1)
CORPORATE SOURCE: (1) Sol Sherry Thrombosis Research Center, Temple University School of Medicine, 3400 North Broad Street, Philadelphia, PA, 19140 USA
SOURCE: Thrombosis and Haemostasis, (Dec., 1999) Vol. 82, No. 6, pp. 1568-1577. ISSN: 0340-6245.
DOCUMENT TYPE: General Review
LANGUAGE: English

L7 ANSWER 12 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS
TI **Inhibition** of **angiogenesis** by two-chain high molecular weight **kininogen** (HKa) is associated with induction of endothelial cell apoptosis.

ACCESSION NUMBER: 2000:46733 BIOSIS
DOCUMENT NUMBER: PREV200000046733
TITLE: **Inhibition** of **angiogenesis** by two-chain high molecular weight **kininogen** (HKa) is associated with induction of endothelial cell apoptosis.
AUTHOR(S): Zhang, Jing-Chuan (1); Sakthivel, Ramasamy (1); Lu, Feng-Min; Darzynkiewicz, Zbigniew; McCrae, Keith R. (1)
CORPORATE SOURCE: (1) Hematology-Oncology, Case Western Reserve University School of Medicine, Cleveland, OH USA
SOURCE: Blood, (Nov. 15, 1999) Vol. 94, No. 10 SUPPL. 1 PART 1, pp. 11a.
Meeting Info.: Forty-first Annual Meeting of the American Society of Hematology New Orleans, Louisiana, USA December

DOCUMENT TYPE: Conference
LANGUAGE: English

L7 ANSWER 13 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS
TI **Inhibition** of tumor **angiogenesis** by a monoclonal
antibody to **kininogen** domain 5.

ACCESSION NUMBER: 2000:46729 BIOSIS

DOCUMENT NUMBER: PREV200000046729

TITLE: **Inhibition** of tumor **angiogenesis** by a
monoclonal antibody to **kininogen** domain 5.

AUTHOR(S): Colman, Robert W. (1); Mousa, Shaker A.

CORPORATE SOURCE: (1) Sol Sherry Thrombosis Research Center, Temple
University School of Medicine, Philadelphia, PA USA
SOURCE: Blood, (Nov. 15, 1999) Vol. 94, No. 10 SUPPL. 1 PART 1,
pp.

10a.

Meeting Info.: Forty-first Annual Meeting of the American
Society of Hematology New Orleans, Louisiana, USA December
3-7, 1999 The American Society of Hematology
. ISSN: 0006-4971.

DOCUMENT TYPE: Conference

LANGUAGE: English

L7 ANSWER 14 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS

TI Two chain high molecular weight **kininogen** **inhibits**
endothelial cell proliferation and **angiogenesis**: Partial
activity within domain 5.

ACCESSION NUMBER: 2000:42551 BIOSIS

DOCUMENT NUMBER: PREV200000042551

TITLE: Two chain high molecular weight **kininogen**
inhibits endothelial cell proliferation and
angiogenesis: Partial activity within domain 5.

AUTHOR(S): Zhang, Jing-Chuan (1); Claffey, Kevin P.; Sakthivel,
Ramasamy (1); Leal, Juan; McCrae, Keith R. (1)

CORPORATE SOURCE: (1) Hematology-Oncology, Case Western Reserve University
School of Medicine, Cleveland, OH USA

SOURCE: Blood, (Nov. 15, 1999) Vol. 94, No. 10 SUPPL. 1 PART 1,
pp.

10a.

Meeting Info.: Forty-first Annual Meeting of the American
Society of Hematology New Orleans, Louisiana, USA December
3-7, 1999 The American Society of Hematology
. ISSN: 0006-4971.

DOCUMENT TYPE: Conference

LANGUAGE: English

L7 ANSWER 15 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS

TI Domain 5 of high molecular weight **kininogen** (kininostatin)
downregulates endothelial cell proliferation and migration and
inhibits angiogenesis.

ACCESSION NUMBER: 1999:308253 BIOSIS

DOCUMENT NUMBER: PREV199900308253

TITLE: Domain 5 of high molecular weight **kininogen**
(kininostatin) downregulates endothelial cell
proliferation

and migration and **inhibits angiogenesis**

AUTHOR(S): Colman, R. W. (1); Jameson, B.; Mousa, S. A.

CORPORATE SOURCE: (1) Sol Sherry Thrombosis Research Center, Temple
University School of Medicine, Philadelphia, PA USA
SOURCE: FASEB Journal, (April 23, 1999) Vol. 13, No. 7, pp.
A1407.

for Meeting Info.: Annual Meeting of the American Societies
Experimental Biology on Biochemistry and Molecular Biology
99 San Francisco, California, USA May 16-20, 1999 American
Societies for Experimental Biology
. ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English

L7 ANSWER 16 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS
TI **Inhibition of angiogenesis** by peptides derived from
kininogen.
ACCESSION NUMBER: 1999:96019 BIOSIS
DOCUMENT NUMBER: PREV199900096019
TITLE: **Inhibition of angiogenesis** by peptides
derived from **kininogen**.
AUTHOR(S): Colman, R. W. (1); Lin, Y.; Johnson, D.; Mousa, S. A.
CORPORATE SOURCE: (1) Sol Sherry Thrombosis Res. Center, Temple Univ. Sch.
Med., Philadelphia, PA USA
SOURCE: Blood, (Nov. 15, 1998) Vol. 92, No. 10 SUPPL. 1 PART 1-2,
pp. 174A.
Meeting Info.: 40th Annual Meeting of the American Society
of Hematology Miami Beach, Florida, USA December 4-8, 1998
The American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English

L7 ANSWER 17 OF 95 USPATFULL
TI DNA fragmentation factor involved in apoptosis
AB The invention provides methods and compositions relating to DNA
Fragmentation Factor (DFF) polypeptides and related nucleic acids. More
particularly, the present invention provides the sequence for the
active
subunit of DFF. The polypeptides may be produced recombinantly from
host cells transformed from the disclosed DFF encoding nucleic acids or
purified from human cells. The invention provides isolated DFF
hybridization probes and primers capable of specifically hybridization
with the disclosed DFF genes, DFF-specific binding agents such as
specific antibodies, and methods of making and using the subject
compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2000:174366 USPATFULL
TITLE: DNA fragmentation factor involved in apoptosis
INVENTOR(S): Wang, Xiaodong, Dallas, TX, United States
Liu, Xuesong, Dallas, TX, United States
PATENT ASSIGNEE(S): The University of Texas System Board of Regents,
Austin, TX, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6165737		20001226
APPLICATION INFO.:	US 1998-61702		19980416 (9)
DOCUMENT TYPE:	Utility		
PRIMARY EXAMINER:	Achutamurthy, Ponnathapu		
ASSISTANT EXAMINER:	Moore, William W.		
LEGAL REPRESENTATIVE:	Fulbright & Jaworski L.L.P.		
NUMBER OF CLAIMS:	20		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	1 Drawing Figure(s); 1 Drawing Page(s)		
LINE COUNT:	5176		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 18 OF 95 USPATFULL

TI Serine protease **inhibitors** comprising .alpha.-keto heterocycles

AB Provided are methods of **inhibiting** the activity of a serine protease using protease **inhibitors** that include an alpha-keto heterocycle in their structure. The methods are useful in the treatment of ischemic heart or treatment of symptoms associated with blood coagulation disorders. Also provided are methods for detecting or quantifying the activity of a serine protease in a pure sample.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2000:167985 USPATFULL

TITLE: Serine protease **inhibitors** comprising .alpha.-keto heterocycles

INVENTOR(S): Gyorkos, Albert C., Westminster, CO, United States
Spruce, Lyle W., Arvada, CO, United States
Leimer, Axel H., Lakewood, CO, United States
Cheronis, John C., Conifer, CO, United States

PATENT ASSIGNEE(S): Cortech, Inc., United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6159938		20001212
APPLICATION INFO.:	US 1997-859242		19970520 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1996-761190, filed on 6 Dec 1996, now patented, Pat. No. US 5807829 which is a continuation-in-part of Ser. No. US 1994-345820, filed on 21 Nov 1994, now patented, Pat. No. US		

5618792

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Russel, Jeffrey E.

LEGAL REPRESENTATIVE: Dechert

NUMBER OF CLAIMS: 77

EXEMPLARY CLAIM: 1

LINE COUNT: 1841

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 19 OF 95 USPATFULL

TI Method for assaying for modulators of cytokines of the TFG .beta. superfamily

AB The invention relates to a method for assaying for the presence of a substance that modulates a cytokine of the TGF.beta. superfamily. A substance which is suspected of modulating a cytokine of the TGF.beta. superfamily and a TGF.beta. binding compound which is not a TGF.beta. receptor and which contains a TRH1 domain, or a portion or mimetic thereof, is reacted with a cytokine of the TGF.beta. superfamily under conditions where the compound, portion or mimetic thereof, and the cytokine are capable of forming a complex. Complexes, free compound and/or cytokine are assayed and compared with a control. The invention also relates to a composition comprising at least one compound which is not a TGF.beta. receptor and which contains the TRH1 domain or a portion, or a mimetic thereof, and a pharmaceutically acceptable carrier, auxiliary or excipient and to methods of treatment using the composition. Further the invention relates to a method of enhancing the activity of growth factors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 1998:134826 USPATFULL

TITLE: Method for assaying for modulators of cytokines of the TFG .beta. superfamily

INVENTOR(S): Dennis, James W., Etobicoke, Canada
Demetriou, Michael, Toronto, Canada

PATENT ASSIGNEE(S): Mount Sinai Hospital Corporation, Toronto, Canada
(non-U.S. corporation)

	NUMBER	KIND	DATE
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PATENT INFORMATION:	US 5830671		19981103
APPLICATION INFO.:	US 1997-854768		19970512 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1994-237715, filed on 4 May 1994		
DOCUMENT TYPE:	Utility		
PRIMARY EXAMINER:	Ulm, John		
ASSISTANT EXAMINER:	Mertz, Prema		
LEGAL REPRESENTATIVE:	Merchant, Gould, Smith, Edell, Welter & Schmidt		
NUMBER OF CLAIMS:	13		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	11 Drawing Figure(s); 11 Drawing Page(s)		
LINE COUNT:	1480		
CAS INDEXING IS AVAILABLE FOR THIS PATENT.			

L7 ANSWER 20 OF 95 USPATFULL

TI Aptamers specific for biomolecules and methods of making
 AB A method for identifying oligomer sequences, optionally comprising modified base, which specifically bind target molecules such as serum proteins, kinins, eicosanoids and extracellular proteins is described. The method is used to generate aptamers that bind to serum Factor X, PDGF, FGF, ICAM, VCAM, E-selectin, thrombin, bradykinin, PGF2 and cell surface molecules. The technique involves complexation of the target molecule with a mixture of oligonucleotides containing random sequences and sequences which serve as primer for PCR under conditions wherein a complex is formed with the specifically binding sequences, but not with the other members of the oligonucleotide mixture. The complex is then separated from uncomplexed oligonucleotides and the complexed members of the oligonucleotide mixture are recovered from the separated complex using the polymerase chain reaction. The recovered oligonucleotides may be sequenced, and successive rounds of selection using complexation, separation, amplification and recovery can be employed. The oligonucleotides can be used for therapeutic and diagnostic purposes and for generating secondary aptamers.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 1998:57716 USPATFULL
 TITLE: Aptamers specific for biomolecules and methods of making
 INVENTOR(S): Griffin, Linda, Atherton, CA, United States
 Albrecht, Glenn, Redwood City, CA, United States
 Latham, John, Palo Alto, CA, United States
 Leung, Lawrence, Hillsborough, CA, United States
 Vermaas, Eric, Oakland, CA, United States
 Toole, John J., Burlingame, CA, United States
 PATENT ASSIGNEE(S): Gilead Sciences, Inc., Foster City, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
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PATENT INFORMATION:	US 5756291		19980526
APPLICATION INFO.:	US 1995-484192		19950607 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1992-934387, filed on 21 Aug 1992, now abandoned		
DOCUMENT TYPE:	Utility		
PRIMARY EXAMINER:	Zitomer, Stephanie W.		
LEGAL REPRESENTATIVE:	Bosse, Mark L.		
NUMBER OF CLAIMS:	12		
EXEMPLARY CLAIM:	1		

NUMBER OF DRAWINGS: 6 Drawing Figure(s); 6 Drawing Page(s)
LINE COUNT: 842
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 21 OF 95 HCAPLUS COPYRIGHT 2001 ACS
TI **Inhibition of angiogenesis** by antibodies against high
molecular weight **kininogen** domain 5
AB Antibodies directed against an antigenic determinant of high mol. wt.
kininogen domain 5, particularly a determinant located in the
region formed by light chain amino acids Gly(440) to Lys(502),
inhibit angiogenesis.

ACCESSION NUMBER: 2001:359837 HCAPLUS

DOCUMENT NUMBER: 134:365709

TITLE: **Inhibition of angiogenesis** by
antibodies against high molecular weight
kininogen domain 5

INVENTOR(S): Colman, Robert W.; Mousa, Shaker A.

PATENT ASSIGNEE(S): Temple University of the Commonwealth System of
Higher

SOURCE: Education, USA; DuPont Pharmaceuticals Company
PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034195	A1	20010517	WO 2000-US30975	20001110
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
PRIORITY APPLN. INFO.:			US 1999-165165	P 19991112
REFERENCE COUNT:	7			
REFERENCE(S):	(3) Hasan; Jnl Biol Chem 1995, V270(33), P19256 HCAPLUS			
	(4) Khan; Am J Physiol 1998, V275(1 Pt 2), PH145 MEDLINE			
	(5) McCrae, R; WO 0027866 2000 HCAPLUS			
	(6) Reddigari; Blood 1993, V81(5), P1306 HCAPLUS			
	(7) Shariat-Madar; Trds Cardio Med 1999, V9(8), P238 HCAPLUS			
	ALL CITATIONS AVAILABLE IN THE RE FORMAT			

L7 ANSWER 22 OF 95 HCAPLUS COPYRIGHT 2001 ACS

TI Role of the light chain of high molecular weight **kininogen** in
adhesion, cell-associated proteolysis and **angiogenesis**

AB A review with 22 refs. Cleavage of high mol. wt. **kininogen** (HK)
by plasma kallikrein results in a light chain and a heavy chain (HK).

The

light chain has two domains: D6, which binds (pre)kallikrein, and D5, which binds to anionic surfaces, including heparin as well as zinc. Initially, HK was thought to be important for surface-activated coagulation. HKa or D5 binds to the urokinase receptor on endothelial cells, thereby enhancing the conversion of prourokinase to urokinase by kallikrein, and, thus, cell-assocd. fibrinolysis. HKa or D5 is antiadhesive by competing with vitronectin binding to the urokinase

receptor and/or forming a complex with vitronectin. D5 **inhibits** endothelial cell migration, proliferation, tube formation and **angiogenesis**, thus modulating inflammation and neovascularization.

ACCESSION NUMBER: 2001:216006 HCAPLUS
DOCUMENT NUMBER: 134:261312
TITLE: Role of the light chain of high molecular weight **kininogen** in adhesion, cell-associated proteolysis and **angiogenesis**

AUTHOR(S): Colman, Robert W.
CORPORATE SOURCE: Sol Sherry Thrombosis Research Center, Temple University School of Medicine, Philadelphia, PA, 19140, USA

SOURCE: Biol. Chem. (2001), 382(1), 65-70
CODEN: BICHF3; ISSN: 1431-6730
PUBLISHER: Walter de Gruyter GmbH & Co. KG
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
REFERENCE COUNT: 22
REFERENCE(S): (1) Chavakis, T; Blood 2000, V96, P514 HCAPLUS
(4) Colman, R; J Clin Invest 1997, V100, P1481

HCAPLUS

(6) Hasan, A; Proc Natl Acad Sci 1998, V95, P3615 HCAPLUS

HCAPLUS

(7) Herwald, H; J Biol Chem 1996, V271, P13040

HCAPLUS

(9) Ichinose, A; J Biol Chem 1986, V261, P3486

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 23 OF 95 HCAPLUS COPYRIGHT 2001 ACS
TI Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits angiogenesis**: partial activity within domain 5
AB We previously reported that the binding of two-chain high mol. wt. **kininogen** (HKa) to endothelial cells may occur through interactions with endothelial urokinase receptors. Since the binding of urokinase to urokinase receptors activates signaling responses and may stimulate mitogenesis, we assessed the effect of HKa binding on endothelial cell proliferation. Unexpectedly, HKa **inhibited** proliferation in response to several growth factors, with 50% **inhibition** caused by .apprx.10 nM HKa. This activity was Zn2+ dependent and not shared by either single-chain high mol. wt. **kininogen** (HK) or low mol. wt. **kininogen**. HKa selectively **inhibited** the proliferation of human umbilical vein and dermal microvascular endothelial cells, but did not affect that of umbilical vein or human aortic smooth muscle cells, trophoblasts, fibroblasts, or carcinoma cells. **Inhibition** of endothelial proliferation by HKa was assocd. with endothelial cell apoptosis and unaffected by antibodies that block the binding of HK or HKa to any of their known endothelial receptors. Recombinant HK domain 5 displayed activity similar to that of HKa. In vivo, HKa **inhibited** neovascularization of s.c. implanted Matrigel plugs, as well as rat corneal **angiogenesis**. These results demonstrate that HKa is a novel **inhibitor** of **angiogenesis**, whose activity is dependent on the unique conformation of the two-chain mol.

ACCESSION NUMBER: 2001:120471 HCAPLUS
DOCUMENT NUMBER: 134:173152
TITLE: Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits angiogenesis**: partial activity within domain 5

AUTHOR(S): Zhang, Jing-Chuan; Claffey, Kevin; Sakthivel, Ramasamy; Darzynkiewicz, Zbigniew; Shaw, David
Elliot;

Keith

Leal, Juan; Wang, Yi-Chun; Lu, Feng-Min; Mccrae,

CORPORATE SOURCE: Hematology-Oncology Division, Case Western Reserve University School of Medicine, Cleveland, OH, 44106-4937, USA

SOURCE: FASEB J. (2000), 14(15), 2589-2600
CODEN: FAJOEC; ISSN: 0892-6638

PUBLISHER: Federation of American Societies for Experimental Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

REFERENCE COUNT: 69

REFERENCE(S): (1) Arends, M; Am J Pathol 1990, V136, P593 HCAPLUS
(2) Asakura, S; J Biochem 1998, V124, P473 HCAPLUS
(3) Asakura, S; J Cell Biol 1992, V116, P465 HCAPLUS
(4) Berrettini, M; Blood 1986, V68, P455 HCAPLUS
(5) Bornstein, P; J Cell Biol 1995, V130, P503

HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 24 OF 95 HCAPLUS COPYRIGHT 2001 ACS

TI Cancer treatment using angiopoietins targeted to aminophospholipids

AB Disclosed is the surprising discovery that aminophospholipids, such as phosphatidylserine and phosphatidylethanolamine, are specific, accessible and stable markers of the luminal surface of tumor blood vessels. The present invention particularly provides therapeutic constructs and conjugates that bind to aminophospholipids and contain angiopoietins, and various methods of specifically delivering angiopoietins to the stably-expressed aminophospholipids of tumor blood vessels, thereby exerting anti-tumor effects. The constructs can include binding ligands or antibodies and antibody fragments against the aminophospholipids. Pharmaceutical compns. and kits contg. the targeting agent-angiopoietin constructs are also claimed; both the formulations and kit can also contain a second anticancer agent.

ACCESSION NUMBER: 2001:50517 HCAPLUS

DOCUMENT NUMBER: 134:105841

TITLE: Cancer treatment using angiopoietins targeted to aminophospholipids

INVENTOR(S): Thorpe, Philip E.

PATENT ASSIGNEE(S): Maine Medical Center Research Institute, USA; Board of Regents, the University of Texas System

SOURCE: PCT Int. Appl., 248 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001003735	A1	20010118	WO 2000-US18779	20000711
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRIORITY APPLN. INFO.:			US 1999-143762	P 19990712
REFERENCE COUNT:		4		
REFERENCE(S):		(1) Godowski; US 6057435 A 2000 HCAPLUS (2) Maisonpierre, P; Science 1997, V277 HCAPLUS (3) Thorpe; US 5776427 A 1998 HCAPLUS (4) Thorpe; US 5855866 A 1999 HCAPLUS		

L7 ANSWER 25 OF 95 HCAPLUS COPYRIGHT 2001 ACS

TI **Inhibition of angiogenesis** by high-molecular-weight **kininogen** domain 3 peptide analogs

AB Peptide analogs the high-mol.-wt. **kininogen** domain 3 are potent **inhibitors of angiogenesis**. The peptides have the formula (a) X1-Asn-Asn-Ala-Thr-Phe-Tyr-Phe-Lys-X2, (b) X3-Cys-Val-Gly-Cys-X4, (c) X5-Leu-Asp-X7-Asn-Ala-Glu-Val-Tyr-X6, or (d) Tyr-Phe-Ile-Asp-Phe-Val-Ala-Arg-Glu-Thr-Thr-X7-Ser-Lys-Glu-Ser (X1-X6 = 0-12 amino acids, more preferably 0-6 amino acids; X7 = Ala, Cys). The peptides may also comprise biol. active fragments of high-mol.-wt. **kininogen** domain 3. Methods of **inhibiting** endothelial cell proliferation and **angiogenesis** are provided.

ACCESSION NUMBER: 2000:420922 HCAPLUS

DOCUMENT NUMBER: 133:68945

TITLE: **Inhibition of angiogenesis** by high-molecular-weight **kininogen** domain 3 peptide analogs

INVENTOR(S): McCrae, R. Keith

PATENT ASSIGNEE(S): Temple University - of the Commonwealth System of Higher Education, USA

SOURCE: PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035407	A2	20000622	WO 1999-US28465	19991202
WO 2000035407	A3	20000908		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000017494	A1	20000703	AU 2000-17494	19991202
PRIORITY APPLN. INFO.:			US 1998-112427	P 19981216
			WO 1999-US28465	W 19991202
OTHER SOURCE(S):		MARPAT 133:68945		

L7 ANSWER 26 OF 95 HCAPLUS COPYRIGHT 2001 ACS

TI **Inhibition of angiogenesis** and endothelial cell proliferation by high-molecular-weight **kininogen** and peptide analogs thereof

AB Two-chain high-mol.-wt. **kininogen**, and peptide analogs thereof having homol. to sites within **kininogen** domain 5, are potent **inhibitors of angiogenesis**. The peptides have the formula X1-His-Lys-X-Lys-X2 (X = any amino acid; X1, X2= 0-12 amino acids,

more preferably 0-6 amino acids, most preferably 0-3 amino acids). X is preferably an amino acid having a nonpolar side chain, or a polar side chain which is uncharged at pH 6.0 to 7.0. X is most preferably Asn, Phe or His. Methods of **inhibiting** endothelial cell proliferation and **angiogenesis** are provided.

ACCESSION NUMBER: 2000:335430 HCAPLUS

DOCUMENT NUMBER: 133:802

TITLE: **Inhibition of angiogenesis** and endothelial cell proliferation by high-molecular-weight **kininogen** and peptide analogs thereof

INVENTOR(S): Mccrae, R. Keith

PATENT ASSIGNEE(S): Temple University - of the Commonwealth System of
Higher Education, USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027866	A1	20000518	WO 1999-US26419	19991105
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 1998-107833 P 19981110	
OTHER SOURCE(S):			MARPAT 133:802	
REFERENCE COUNT:			10	
REFERENCE(S):			(1) Dennis; US 5830671 A 1998 HCAPLUS (2) Griffin; US 5756291 A 1998 HCAPLUS (3) Guerinot; US 5846821 A 1998 HCAPLUS (4) Heitsch; US 5786365 A 1998 HCAPLUS (7) Lottspeich; European Journal of Biochemistry	

1985,

V152, P307 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 27 OF 95 HCAPLUS COPYRIGHT 2001 ACS
 TI **Inhibition of angiogenesis** by peptide analogs of
 high-molecular-weight **kininogen** domain 5
 AB A method for **inhibition** of endothelial cell proliferation in a
 mammal comprises peptides and proteins of high-mol.-wt. **kininogen**
 light chain (domain 5). For example, glutathione-S-transferase (GST)
 fusion proteins with high-mol.-wt. **kininogen** light chain
 peptides, i.e. Lys(420)-Ser(513) (SEQ ID NO: 10) and His(441)-Ser(626)
 (SEQ ID NO: 8), at concns. of 0.27 and 0.39 .mu.M, resp. induced 100%
inhibition of proliferation of human umbilical vein endothelial
 cells (HUVEC). Also, GST-SEQ ID NO: 10 at a concn. of 0.27 .mu.M
 achieved
 100% **inhibition** of HUVEC migration to vitronectin.
 ACCESSION NUMBER: 2000:335256 HCAPLUS
 DOCUMENT NUMBER: 132:343359
 TITLE: **Inhibition of angiogenesis** by
 peptide analogs of high-molecular-weight
kininogen domain 5
 INVENTOR(S): Colman, W. Robert; Mousa, A. Shaker
 PATENT ASSIGNEE(S): Temple University - of the Commonwealth System of
 Higher Education, USA; Dupont Pharmaceuticals Company
 SOURCE: PCT Int. Appl., 41 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027415	A2	20000518	WO 1999-US26377	19991109

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1044012 A1 20001018 EP 1999-957529 19991109

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1998-107844 P 19981110
WO 1999-US26377 W 19991109

L7 ANSWER 28 OF 95 HCAPLUS COPYRIGHT 2001 ACS

TI Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and **inhibits angiogenesis**

AB We have demonstrated that high mol. wt. **kininogen** (HK) binds specifically on endothelial cells to domain 2/3 of the urokinase receptor (uPAR). **Inhibition** by vitronectin suggests that kallikrein-cleaved HK (HKa) is antiadhesive. Plasma kallikrein bound to HK cleaves prourokinase to urokinase, initiating cell-assocd. fibrinolysis. We postulated that HK cell binding domains would **inhibit angiogenesis**. We found that recombinant domain 5 (D5) **inhibited** endothelial cell migration toward vitronectin 85% at 0.27 .mu.M with an IC50 (concn. to yield 50% **inhibition**) = 0.12 .mu.M. A D5 peptide, G486-K502, showed an IC50 = 0.2 .mu.M, but a 25-mer peptide from a D3 cell binding domain only **inhibited** migration 10% at 139 .mu.M (IC50 > 50 .mu.M). D6 exhibited weaker **inhibitory** activity (IC50 = 0.50 .mu.M). D5 also potently **inhibited** endothelial cell proliferation with an IC50 = 30 nM, while D3 and D6 were inactive. Using deletion mutants of D5, we localized the smallest region for full activity to H441-D474. To further map the active region, we created a mol. homol. model of D5 and designed a series of peptides displaying surface loops. Peptide 440-455 was the most potent (IC50 = 100 nM) in **inhibiting** proliferation but did not **inhibit** migration. D5 **inhibited angiogenesis** stimulated by fibroblast growth factor FGF2 (97%) in a chicken chorioallantoic membrane assay at 270 nM, and peptide 400-455 was also **inhibitory** (79%). HK D5 (for which we suggest the designation, "kininostatin") is a potent **inhibitor** of endothelial cell migration and proliferation in vitro and of **angiogenesis** in vivo.

ACCESSION NUMBER: 2000:55516 HCAPLUS

DOCUMENT NUMBER: 132:164060

TITLE: Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and **inhibits angiogenesis**

AUTHOR(S): Colman, Robert W.; Jameson, Bradford A.; Lin, Yingzhang; Johnson, Donald; Mousa, Shaker A.

CORPORATE SOURCE: Sol Sherry Thrombosis Research Center, Temple University School of Medicine, Philadelphia, PA, USA

SOURCE: Blood (2000), 95(2), 543-550
CODEN: BLOOAW; ISSN: 0006-4971

PUBLISHER: American Society of Hematology

DOCUMENT TYPE: Journal

LANGUAGE: English

REFERENCE COUNT: 52

REFERENCE(S): (1) Asakura, S; J Cell Biol 1992, V116, P465 HCAPLUS

(3) Bacharach, E; Proc Natl Acad Sci U S A 1992, V89, P10686 HCAPLUS

(4) Barnathan, E; Blood 1990, V7 P1795 HCAPLUS

(5) Behrendt, N; J Biol Chem 1991, V266, P7842

HCAPLUS

(7) Bradford, H; Blood 1997, V90, P1508 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 29 OF 95 HCAPLUS COPYRIGHT 2001 ACS

TI Biologic activities of the contact factors in vivo. Potentiation of hypotension, inflammation, and fibrinolysis, and **inhibition** of cell adhesion, **angiogenesis**, and thrombosis

AB A review with 127 refs. is given on the biol. roles of contact factors, particularly the in vivo functions. Bradykinin is released from high mol.

wt. prekallikrein (PK) and low mol. wt. **kininogen** (LK) helps to regulate blood pressure under physiol. conditions, whereas in systemic inflammatory response syndrome (SIRS) it is an important contributor to pathol. hypotension. Bradykinin is also important in acute inflammatory disease, but a larger role is played by blood plasma kallikrein, which

not

only releases bradykinin, but acts directly as an agonist for neutrophils,

causing release of elastase, chemotaxis, neutrophil aggregation, and superoxide prodn. New studies involving the contact system interactions with endothelial cells and leukocytes emphasize the role of high mol. wt. **kininogen** (HK) and PK in the initiation of cell-assocd. plasmin formation. HK was also characterized as a counter-adhesive protein, **inhibiting** neutrophil-fibrinogen binding interactions and endothelial adhesion to vitronectin. The domain 5 of HK as well as peptides derived from the domain serve as potent **inhibitors** of **angiogenesis** in vivo, blocking both endothelial cell migration to vitronectin and endothelial cell proliferation. Both clin. (factor XIII deficiency) and expt. animal models (**kininogen** deficiency) suggest that HK and/or LK are antithrombotic mols., and that the contact system serves as an anticoagulant, profibrinolytic system. Although

FXII,

PK, and HK each have multiple domains and functions, the system clearly exists to keep vessels patent, and peptides or recombinant fragments may serve as modulators of blood pressure, inflammation, and fibrinolysis, as well as influencing cell adhesion, **angiogenesis**, and the thrombotic process.

ACCESSION NUMBER: 1999:803232 HCAPLUS

DOCUMENT NUMBER: 132:48325

TITLE: Biologic activities of the contact factors in vivo. Potentiation of hypotension, inflammation, and fibrinolysis, and **inhibition** of cell adhesion, **angiogenesis**, and thrombosis

AUTHOR(S): Colman, Robert W.

CORPORATE SOURCE: Sol Sherry Thrombosis Research Center, School Medicine, Temple Univ., Philadelphia, PA, 19140, USA
Thromb. Haemostasis (1999), 82(6), 1568-1577

SOURCE: CODEN: THHADQ; ISSN: 0340-6245

PUBLISHER: F. K. Schattauer Verlagsgesellschaft mbH

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

REFERENCE COUNT: 127

REFERENCE(S):

(1) Alfie, M; Biochemical & Biophysical Research Communications 1996, V224(3), P625 HCAPLUS

(3) Asakura, S; J Cell Biol 1992, V116, P465 HCAPLUS

(4) Beutler, B; N Engl J Med 1987, V316, P379 HCAPLUS

(6) Blais, C; Arthritis Rheum 1997, V40, P1327

HCAPLUS

(8) Borkowski, J; Canadian Journal of Physiology &

L7 ANSWER 30 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using
compound that **inhibit** endothelial cell migration -
AB The present sequence represents an analogue of the light chain of human
high molecular weight **kininogen**. High molecular weight
kininogen is a 120 kDa glycoprotein which binds with high
affinity to endothelial cells, where it is cleaved by plasma kallikrein
into heavy and light chains. Analogues of high molecular weight
kininogen are used in the method of the invention. The
specification describes a method of **inhibiting** endothelial cell
proliferation. The method comprises contacting endothelial cells with a
compound containing high molecular weight **kininogen** analogues.
The method and the compounds can be used for **inhibiting**
endothelial cell proliferation. The compounds can also be used for
inhibiting angiogenesis. The compounds can also be used
to **inhibit** migration of endothelial cells to vitronectin.
ACCESSION NUMBER: AAY93353 peptide DGENE
TITLE: Method for **inhibiting** endothelial cell
proliferation, using compound that **inhibit**
endothelial cell migration -
INVENTOR: Colman W R; Mousa A S
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(DUPO) DUPONT PHARM CO.
(COLM-I) COLMAN W R.
(MOUS-I) MOUSA A S.
PATENT INFO: WO 2000027415 A2 20000518 41p
APPLICATION INFO: WO 1999-US26377 19991109
PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 31 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using
compound that **inhibit** endothelial cell migration -
AB The present sequence represents an analogue of the light chain of human
high molecular weight **kininogen**. High molecular weight
kininogen is a 120 kDa glycoprotein which binds with high
affinity to endothelial cells, where it is cleaved by plasma kallikrein
into heavy and light chains. Analogues of high molecular weight
kininogen are used in the method of the invention. The
specification describes a method of **inhibiting** endothelial cell
proliferation. The method comprises contacting endothelial cells with a
compound containing high molecular weight **kininogen** analogues.
The method and the compounds can be used for **inhibiting**
endothelial cell proliferation. The compounds can also be used for
inhibiting angiogenesis. The compounds can also be used
to **inhibit** migration of endothelial cells to vitronectin.
ACCESSION NUMBER: AAY93352 peptide DGENE
TITLE: Method for **inhibiting** endothelial cell
proliferation, using compound that **inhibit**
endothelial cell migration -
INVENTOR: Colman W R; Mousa A S
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(DUPO) DUPONT PHARM CO.
(COLM-I) COLMAN W R.
(MOUS-I) MOUSA A S.
PATENT INFO: WO 2000027415 A2 20000518 41p
APPLICATION INFO: WO 1999-US26377 19991109
PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent

LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 32 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using
compound that **inhibit** endothelial cell migration -
AB The present sequence represents an analogue of the light chain of human
high molecular weight **kininogen**. High molecular weight
kininogen is a 120 kDa glycoprotein which binds with high
affinity to endothelial cells, where it is cleaved by plasma kallikrein
into heavy and light chains. Analogues of high molecular weight
kininogen are used in the method of the invention. The
specification describes a method of **inhibiting** endothelial cell
proliferation. The method comprises contacting endothelial cells with a
compound containing high molecular weight **kininogen** analogues.
The method and the compounds can be used for **inhibiting**
endothelial cell proliferation. The compounds can also be used for
inhibiting angiogenesis. The compounds can also be used
to **inhibit** migration of endothelial cells to vitronectin.

ACCESSION NUMBER: AAY93351 peptide DGENE
TITLE: Method for **inhibiting** endothelial cell
proliferation, using compound that **inhibit**
endothelial cell migration -
INVENTOR: Colman W R; Mousa A S
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(DUPO) DUPONT PHARM CO.
(COLM-I) COLMAN W R.
(MOUS-I) MOUSA A S.
PATENT INFO: WO 2000027415 A2 20000518 41p
APPLICATION INFO: WO 1999-US26377 19991109
PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 33 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using
compound that **inhibit** endothelial cell migration -
AB The present sequence represents an analogue of the light chain of human
high molecular weight **kininogen**. High molecular weight
kininogen is a 120 kDa glycoprotein which binds with high
affinity to endothelial cells, where it is cleaved by plasma kallikrein
into heavy and light chains. Analogues of high molecular weight
kininogen are used in the method of the invention. The
specification describes a method of **inhibiting** endothelial cell
proliferation. The method comprises contacting endothelial cells with a
compound containing high molecular weight **kininogen** analogues.
The method and the compounds can be used for **inhibiting**
endothelial cell proliferation. The compounds can also be used for
inhibiting angiogenesis. The compounds can also be used
to **inhibit** migration of endothelial cells to vitronectin.

ACCESSION NUMBER: AAY93350 peptide DGENE
TITLE: Method for **inhibiting** endothelial cell
proliferation, using compound that **inhibit**
endothelial cell migration -
INVENTOR: Colman W R; Mousa A S
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(DUPO) DUPONT PHARM CO.
(COLM-I) COLMAN W R.
(MOUS-I) MOUSA A S.
PATENT INFO: WO 2000027415 A2 20000518 41p
APPLICATION INFO: WO 1999-US26377 19991109
PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent

LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 34 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using
compound that **inhibit** endothelial cell migration -
AB The present sequence represents an analogue of the light chain of human
high molecular weight **kininogen**. High molecular weight
kininogen is a 120 kDa glycoprotein which binds with high
affinity to endothelial cells, where it is cleaved by plasma kallikrein
into heavy and light chains. Analogues of high molecular weight
kininogen are used in the method of the invention. The
specification describes a method of **inhibiting** endothelial cell
proliferation. The method comprises contacting endothelial cells with a
compound containing high molecular weight **kininogen** analogues.
The method and the compounds can be used for **inhibiting**
endothelial cell proliferation. The compounds can also be used for
inhibiting angiogenesis. The compounds can also be used
to **inhibit** migration of endothelial cells to vitronectin.
ACCESSION NUMBER: AAY93349 peptide DGENE
TITLE: Method for **inhibiting** endothelial cell
proliferation, using compound that **inhibit**
endothelial cell migration -
INVENTOR: Colman W R; Mousa A S
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(DUPO) DUPONT PHARM CO.
(COLM-I) COLMAN W R.
(MOUS-I) MOUSA A S.
PATENT INFO: WO 2000027415 A2 20000518 41p
APPLICATION INFO: WO 1999-US26377 19991109
PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 35 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using
compound that **inhibit** endothelial cell migration -
AB The present sequence represents an analogue of the light chain of human
high molecular weight **kininogen**. High molecular weight
kininogen is a 120 kDa glycoprotein which binds with high
affinity to endothelial cells, where it is cleaved by plasma kallikrein
into heavy and light chains. Analogues of high molecular weight
kininogen are used in the method of the invention. The
specification describes a method of **inhibiting** endothelial cell
proliferation. The method comprises contacting endothelial cells with a
compound containing high molecular weight **kininogen** analogues.
The method and the compounds can be used for **inhibiting**
endothelial cell proliferation. The compounds can also be used for
inhibiting angiogenesis. The compounds can also be used
to **inhibit** migration of endothelial cells to vitronectin.
ACCESSION NUMBER: AAY93348 peptide DGENE
TITLE: Method for **inhibiting** endothelial cell
proliferation, using compound that **inhibit**
endothelial cell migration -
INVENTOR: Colman W R; Mousa A S
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(DUPO) DUPONT PHARM CO.
(COLM-I) COLMAN W R.
(MOUS-I) MOUSA A S.
PATENT INFO: WO 2000027415 A2 20000518 41p
APPLICATION INFO: WO 1999-US26377 19991109
PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent

LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 36 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using
compound that **inhibit** endothelial cell migration -
AB The present sequence represents an analogue of the light chain of human
high molecular weight **kininogen**. High molecular weight
kininogen is a 120 kDa glycoprotein which binds with high
affinity to endothelial cells, where it is cleaved by plasma kallikrein
into heavy and light chains. Analogues of high molecular weight
kininogen are used in the method of the invention. The
specification describes a method of **inhibiting** endothelial cell
proliferation. The method comprises contacting endothelial cells with a
compound containing high molecular weight **kininogen** analogues.
The method and the compounds can be used for **inhibiting**
endothelial cell proliferation. The compounds can also be used for
inhibiting angiogenesis. The compounds can also be used
to **inhibit** migration of endothelial cells to vitronectin.

ACCESSION NUMBER: AAY93347 peptide DGENE
TITLE: Method for **inhibiting** endothelial cell
proliferation, using compound that **inhibit**
endothelial cell migration -
INVENTOR: Colman W R; Mousa A S
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(DUPO) DUPONT PHARM CO.
(COLM-I) COLMAN W R.
(MOUS-I) MOUSA A S.
PATENT INFO: WO 2000027415 A2 20000518 41p
APPLICATION INFO: WO 1999-US26377 19991109
PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 37 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using
compound that **inhibit** endothelial cell migration -
AB The present sequence represents an analogue of the light chain of human
high molecular weight **kininogen**. High molecular weight
kininogen is a 120 kDa glycoprotein which binds with high
affinity to endothelial cells, where it is cleaved by plasma kallikrein
into heavy and light chains. Analogues of high molecular weight
kininogen are used in the method of the invention. The
specification describes a method of **inhibiting** endothelial cell
proliferation. The method comprises contacting endothelial cells with a
compound containing high molecular weight **kininogen** analogues.
The method and the compounds can be used for **inhibiting**
endothelial cell proliferation. The compounds can also be used for
inhibiting angiogenesis. The compounds can also be used
to **inhibit** migration of endothelial cells to vitronectin.

ACCESSION NUMBER: AAY93346 peptide DGENE
TITLE: Method for **inhibiting** endothelial cell
proliferation, using compound that **inhibit**
endothelial cell migration -
INVENTOR: Colman W R; Mousa A S
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(DUPO) DUPONT PHARM CO.
(COLM-I) COLMAN W R.
(MOUS-I) MOUSA A S.
PATENT INFO: WO 2000027415 A2 20000518 41p
APPLICATION INFO: WO 1999-US26377 19991109
PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent

LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 38 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using
compound that **inhibit** endothelial cell migration -
AB The present sequence represents a fragment of the light chain of human
high molecular weight **kininogen**. It is used to produce
compounds of the invention. High molecular weight **kininogen** is
a 120 kDa glycoprotein which binds with high affinity to endothelial
cells, where it is cleaved by plasma kallikrein into heavy and light
chains. Analogues of high molecular weight **kininogen** are used
in the method of the invention. The specification describes a method of
inhibiting endothelial cell proliferation. The method comprises
contacting endothelial cells with a compound containing high molecular
weight **kininogen** analogues. The method and the compounds can be
used for **inhibiting** endothelial cell proliferation. The
compounds can also be used for **inhibiting angiogenesis**
. The compounds can also be used to **inhibit** migration of
endothelial cells to vitronectin.

ACCESSION NUMBER: AAY93345 peptide DGENE
TITLE: Method for **inhibiting** endothelial cell
proliferation, using compound that **inhibit**
endothelial cell migration -
INVENTOR: Colman W R; Mousa A S
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(DUPO) DUPONT PHARM CO.
(COLM-I) COLMAN W R.
(MOUS-I) MOUSA A S.
PATENT INFO: WO 2000027415 A2 20000518 41p
APPLICATION INFO: WO 1999-US26377 19991109
PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 39 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using
compound that **inhibit** endothelial cell migration -
AB The present sequence represents a fragment of the light chain of human
high molecular weight **kininogen**. It is used to produce
compounds of the invention. High molecular weight **kininogen** is
a 120 kDa glycoprotein which binds with high affinity to endothelial
cells, where it is cleaved by plasma kallikrein into heavy and light
chains. Analogues of high molecular weight **kininogen** are used
in the method of the invention. The specification describes a method of
inhibiting endothelial cell proliferation. The method comprises
contacting endothelial cells with a compound containing high molecular
weight **kininogen** analogues. The method and the compounds can be
used for **inhibiting** endothelial cell proliferation. The
compounds can also be used for **inhibiting angiogenesis**
. The compounds can also be used to **inhibit** migration of
endothelial cells to vitronectin.

ACCESSION NUMBER: AAY93344 peptide DGENE
TITLE: Method for **inhibiting** endothelial cell
proliferation, using compound that **inhibit**
endothelial cell migration -
INVENTOR: Colman W R; Mousa A S
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(DUPO) DUPONT PHARM CO.
(COLM-I) COLMAN W R.
(MOUS-I) MOUSA A S.
PATENT INFO: WO 2000027415 A2 20000518 41p
APPLICATION INFO: WO 1999-US26377 19991109

PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 40 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using
compound that **inhibit** endothelial cell migration -
AB The present sequence represents an analogue of the light chain of human
high molecular weight **kininogen**. High molecular weight
kininogen is a 120 kDa glycoprotein which binds with high
affinity to endothelial cells, where it is cleaved by plasma kallikrein
into heavy and light chains. Analogues of high molecular weight
kininogen are used in the method of the invention. The
specification describes a method of **inhibiting** endothelial cell
proliferation. The method comprises contacting endothelial cells with a
compound containing high molecular weight **kininogen** analogues.
The method and the compounds can be used for **inhibiting**
endothelial cell proliferation. The compounds can also be used for
inhibiting angiogenesis. The compounds can also be used
to **inhibit** migration of endothelial cells to vitronectin.

ACCESSION NUMBER: AAY93343 peptide DGENE

TITLE: Method for **inhibiting** endothelial cell
proliferation, using compound that **inhibit**
endothelial cell migration -

INVENTOR: Colman W R; Mousa A S

PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.

(DUPO) DUPONT PHARM CO.

(COLM-I) COLMAN W R.

(MOUS-I) MOUSA A S.

PATENT INFO: WO 2000027415 A2 20000518

41p

APPLICATION INFO: WO 1999-US26377 19991109

PRIORITY INFO: US 1998-107844 19981110

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 41 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using
compound that **inhibit** endothelial cell migration -
AB The present sequence represents the light chain of human high molecular
weight **kininogen**. High molecular weight **kininogen** is
a 120 kDa glycoprotein which binds with high affinity to endothelial
cells, where it is cleaved by plasma kallikrein into heavy and light
chains. Analogues of high molecular weight **kininogen** are used
in the method of the invention. The specification describes a method of
inhibiting endothelial cell proliferation. The method comprises
contacting endothelial cells with a compound containing high molecular
weight **kininogen** analogues. The method and the compounds can be
used for **inhibiting** endothelial cell proliferation. The
compounds can also be used for **inhibiting angiogenesis**
. The compounds can also be used to **inhibit** migration of
endothelial cells to vitronectin.

ACCESSION NUMBER: AAY93342 protein DGENE

TITLE: Method for **inhibiting** endothelial cell
proliferation, using compound that **inhibit**
endothelial cell migration -

INVENTOR: Colman W R; Mousa A S

PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.

(DUPO) DUPONT PHARM CO.

(COLM-I) COLMAN W R.

(MOUS-I) MOUSA A S.

PATENT INFO: WO 2000027415 A2 20000518

41p

APPLICATION INFO: WO 1999-US26377 19991109

PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 42 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and
endothelial cell proliferation, inducing endothelial cell apoptosis and
treating cancer, rheumatoid arthritis, and ocular disorders comprises a
kininogen domain 3 analog -
AB The present sequence is that of a D3 peptide derived from high mol.wt.
kininogen (HK) domain 3 (see AAY95426). The D3 peptide, which
may optionally include N-terminal and/or C-terminal protecting groups,
inhibits endothelial cell proliferation and thus possesses
anti-angiogenic activity. It is an example of peptides of the invention
(see AAY95405-26) which are analogues of certain sites in the HK domain
3, in this case amino acids Leu331-Tyr338, and in which cysteine
residues
may be replaced by alanine residues. The peptides **inhibit**
endothelial cell proliferation and may also induce endothelial cell
apoptosis. Compositions including such peptides are used in claimed
methods for **inhibiting angiogenesis**,
inhibiting endothelial cell proliferation, and inducing
endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular
disorders characterized by undesired vascularization of the retina are
treated.

ACCESSION NUMBER: AAY95427 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis**
and endothelial cell proliferation, inducing endothelial
cell
apoptosis and treating cancer, rheumatoid arthritis, and
ocular disorders comprises a **kininogen** domain 3
analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 43 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and
endothelial cell proliferation, inducing endothelial cell apoptosis and
treating cancer, rheumatoid arthritis, and ocular disorders comprises a
kininogen domain 3 analog -
AB The present sequence is that of domain 3 of human high mol.wt.
kininogen (HK). The invention provides peptides (see
AAY95405-24) that are analogues of certain sites in the HK domain 3,
specifically Asn275-Lys282, Cys246-Cys249, Leu331-Tyr338 and
Tyr299-Ser314. The peptides, in which native Cys residues may be
replaced by Ala residues, **inhibit** endothelial cell
proliferation and may also induce endothelial cell apoptosis.
Compositions including the peptides are used in claimed methods for
inhibiting angiogenesis, **inhibiting**
endothelial cell proliferation, and inducing endothelial cell apoptosis.
Cancer, rheumatoid arthritis, and ocular disorders characterized by
undesired vascularization of the retina are treated.
ACCESSION NUMBER: AAY95426 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis**
and endothelial cell proliferation, inducing endothelial
cell

apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog

INVENTOR: McCrae R K
 PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
 (MCCR-I) MCCRAE R K.
 PATENT INFO: WO 2000035407 A2 20000622 44p
 APPLICATION INFO: WO 1999-US28465 19991202
 PRIORITY INFO: US 1998-112427 19981216
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 44 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
 AB The present sequence is that of a D3 peptide derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the
 HK domain 3, in this case amino acid residues Cys246-Cys249. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95425 Peptide DGENE
 TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell

apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -

INVENTOR: McCrae R K
 PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
 (MCCR-I) MCCRAE R K.
 PATENT INFO: WO 2000035407 A2 20000622 44p
 APPLICATION INFO: WO 1999-US28465 19991202
 PRIORITY INFO: US 1998-112427 19981216
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 45 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
 AB The present sequence is that of a C-terminal fragment of a novel anti-angiogenic D3 peptide (see AAY95416) derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95428). The full-length D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of peptides of the invention (see AAY95405-26) that are analogues of certain sites in the
 HK domain 3. The peptides **inhibit** endothelial cell proliferation

and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis, inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95424 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis**
and endothelial cell proliferation, inducing endothelial
cell apoptosis and treating cancer, rheumatoid arthritis, and
ocular disorders comprises a **kininogen** domain 3
analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 46 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and
endothelial cell proliferation, inducing endothelial cell apoptosis and
treating cancer, rheumatoid arthritis, and ocular disorders comprises a
kininogen domain 3 analog -
AB The present sequence is that of a D3 peptide derived from human high
mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide
inhibits endothelial cell proliferation and thus possesses
anti-angiogenic activity. It is an example of D3 peptides of the
invention (see AAY95405-26) that are analogues of certain sites in the
HK domain 3, in this case Tyr299-Ser314, and in which native cysteine
residues may be replaced by alanine residues. The peptides
inhibit endothelial cell proliferation and may also induce
endothelial cell apoptosis. Compositions including the peptides are
used in claimed methods for **inhibiting angiogenesis,**
inhibiting endothelial cell proliferation, and inducing
endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular
disorders characterized by undesired vascularization of the retina are
treated. The IC50 value for the present peptide was 28 uM for
inhibition of fibroblast growth factor-induced HUVEC cell
proliferation.

ACCESSION NUMBER: AAY95423 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis**
and endothelial cell proliferation, inducing endothelial
cell apoptosis and treating cancer, rheumatoid arthritis, and
ocular disorders comprises a **kininogen** domain 3
analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 47 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -

AB The present sequence is that of a D3 peptide derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the

HK domain 3, in this case Tyr299-Ser314, and in which native cysteine residues may be replaced by alanine residues. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95422 Peptide DGENE
 TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
 INVENTOR: McCrae R K
 PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
 (MCCR-I) MCCRAE R K.
 PATENT INFO: WO 2000035407 A2 20000622 44p
 APPLICATION INFO: WO 1999-US28465 19991202
 PRIORITY INFO: US 1998-112427 19981216
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 48 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -

AB The present sequence is that of a D3 peptide derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the

HK domain 3, in this case amino acid residues Leu331-Tyr338, and in which native cysteine residues may be replaced by alanine residues. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated. The IC50 value for the present peptide was 44 uM for **inhibition** of fibroblast growth factor-induced HUVEC cell proliferation.

ACCESSION NUMBER: AAY95421 Peptide DGENE
 TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and

ocular disorders comprises a **kininogen** domain 3 analog -
 INVENTOR: McCrae R K
 PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
 (MCCR-I) MCCRAE R K.
 PATENT INFO: WO 2000035407 A2 20000622 44p
 APPLICATION INFO: WO 1999-US28465 19991202
 PRIORITY INFO: US 1998-112427 19981216
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 49 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -

AB The present sequence is that of a D3 peptide derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the

HK domain 3, in this case amino acid residues Leu331-Tyr338, and in which native cysteine residues may be replaced by alanine residues. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated. The IC50 value for the present peptide was 42 uM for **inhibition** of fibroblast growth factor-induced HUVEC cell proliferation.

ACCESSION NUMBER: AAY95420 Peptide DGENE
 TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell

apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -

INVENTOR: McCrae R K
 PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
 (MCCR-I) MCCRAE R K.
 PATENT INFO: WO 2000035407 A2 20000622 44p
 APPLICATION INFO: WO 1999-US28465 19991202
 PRIORITY INFO: US 1998-112427 19981216
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 50 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -

AB The present sequence is that of a D3 peptide derived from high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide, which may optionally include N-terminal and/or C-terminal protecting groups, **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of peptides of the invention (see AAY95405-26) which are analogues of certain sites in the HK domain 3, in this case amino acids Leu331-Tyr338, and in which cysteine residues

may be replaced by alanine residues. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including such peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95419 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis**
and endothelial cell proliferation, inducing endothelial
cell apoptosis and treating cancer, rheumatoid arthritis, and
ocular disorders comprises a **kininogen** domain 3
analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 51 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and
endothelial cell proliferation, inducing endothelial cell apoptosis and
treating cancer, rheumatoid arthritis, and ocular disorders comprises a
kininogen domain 3 analog -
AB The present sequence is that of a D3 peptide derived from human high
mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide
inhibits endothelial cell proliferation and thus possesses
anti-angiogenic activity. It is an example of D3 peptides of the
invention (see AAY95405-26) that are analogues of certain sites in the
HK domain 3, in this case amino acid residues Leu331-Tyr338, where native
cysteine residues may be replaced by alanine residues. The peptides
inhibit endothelial cell proliferation and may also induce
endothelial cell apoptosis. Compositions including the peptides are
used in claimed methods for **inhibiting angiogenesis**,
inhibiting endothelial cell proliferation, and inducing
endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular
disorders characterized by undesired vascularization of the retina are
treated.

ACCESSION NUMBER: AAY95418 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis**
and endothelial cell proliferation, inducing endothelial
cell apoptosis and treating cancer, rheumatoid arthritis, and
ocular disorders comprises a **kininogen** domain 3
analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 52 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -

AB The present sequence is that of an N-terminal fragment of a novel anti-angiogenic D3 peptide (see AAY95418) derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The full-length D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of peptides of the invention (see AAY95405-26) that are analogues of certain sites in the

HK domain 3. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis, inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95417 Peptide DGENE

TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -

INVENTOR: McCrae R K

PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.

PATENT INFO: WO 2000035407 A2 20000622 44p

APPLICATION INFO: WO 1999-US28465 19991202

PRIORITY INFO: US 1998-112427 19981216

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 53 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -

AB The present sequence is that of a D3 peptide derived from high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide, which may optionally include N-terminal and/or C-terminal protecting groups, **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of peptides of the invention (see AAY95405-26) which are analogues of certain sites in the HK domain 3, in this case amino acids Leu331-Tyr338, and in which cysteine residues may be replaced by alanine residues. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including such peptides are used in claimed methods for **inhibiting angiogenesis, inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95416 Peptide DGENE

TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -

INVENTOR: McCrae R K
 PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
 (MCCR-I) MCCRAE R K.
 PATENT INFO: WO 2000035407 A2 20000622 44p
 APPLICATION INFO: WO 1999-US28465 19991202
 PRIORITY INFO: US 1998-112427 19981216
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 54 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 TI Composition for **inhibiting angiogenesis** and
 endothelial cell proliferation, inducing endothelial cell apoptosis and
 treating cancer, rheumatoid arthritis, and ocular disorders comprises a
kininogen domain 3 analog -
 AB The present sequence is that of a D3 peptide derived from human high
 mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide
inhibits endothelial cell proliferation and thus possesses
 anti-angiogenic activity. It is an example of D3 peptides of the
 invention (see AAY95405-26) that are analogues of certain sites in the
 HK domain 3, in this case amino acid residues Cys246-Cys249. The peptides
inhibit endothelial cell proliferation and may also induce
 endothelial cell apoptosis. Compositions including the peptides are
 used in claimed methods for **inhibiting angiogenesis**,
inhibiting endothelial cell proliferation, and inducing
 endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular
 disorders characterized by undesired vascularization of the retina are
 treated. The IC50 value for the present peptide was 30 uM for
inhibition of fibroblast growth factor-induced HUVEC cell
 proliferation.

ACCESSION NUMBER: AAY95415 Peptide DGENE
 TITLE: Composition for **inhibiting angiogenesis**
 and endothelial cell proliferation, inducing endothelial
 cell apoptosis and treating cancer, rheumatoid arthritis, and
 ocular disorders comprises a **kininogen** domain 3
 analog -

INVENTOR: McCrae R K
 PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
 (MCCR-I) MCCRAE R K.
 PATENT INFO: WO 2000035407 A2 20000622 44p
 APPLICATION INFO: WO 1999-US28465 19991202
 PRIORITY INFO: US 1998-112427 19981216
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 55 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 TI Composition for **inhibiting angiogenesis** and
 endothelial cell proliferation, inducing endothelial cell apoptosis and
 treating cancer, rheumatoid arthritis, and ocular disorders comprises a
kininogen domain 3 analog -
 AB The present sequence is that of a D3 peptide derived from human high
 mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide
inhibits endothelial cell proliferation and thus possesses
 anti-angiogenic activity. It is an example of D3 peptides of the
 invention (see AAY95405-26) that are analogues of certain sites in the
 HK domain 3, in this case amino acid residues Cys246-Cys249. The peptides
inhibit endothelial cell proliferation and may also induce
 endothelial cell apoptosis. Compositions including the peptides are
 used

in claimed methods for **inhibiting angiogenesis**,
inhibiting endothelial cell proliferation, and inducing
endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular
disorders characterized by undesired vascularization of the retina are
treated.

ACCESSION NUMBER: AAY95414 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis**
and endothelial cell proliferation, inducing endothelial
cell
apoptosis and treating cancer, rheumatoid arthritis, and
ocular disorders comprises a **kininogen** domain 3
analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 56 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and
endothelial cell proliferation, inducing endothelial cell apoptosis and
treating cancer, rheumatoid arthritis, and ocular disorders comprises a
kininogen domain 3 analog -
AB The present sequence is that of a C-terminal fragment of a novel
anti-angiogenic D3 peptide (see AAY95414) derived from human high
mol.wt.
kininogen (HK) domain 3 (see AAY95426). The full-length D3
peptide **inhibits** endothelial cell proliferation and thus
possesses anti-angiogenic activity. It is an example of peptides of the
invention (see AAY95405-26) that are analogues of certain sites in the
HK
domain 3. The peptides **inhibit** endothelial cell proliferation
and may also induce endothelial cell apoptosis. Compositions including
the peptides are used in claimed methods for **inhibiting**
angiogenesis, **inhibiting** endothelial cell
proliferation, and inducing endothelial cell apoptosis. Cancer,
rheumatoid arthritis, and ocular disorders characterized by undesired
vascularization of the retina are treated.

ACCESSION NUMBER: AAY95413 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis**
and endothelial cell proliferation, inducing endothelial
cell
apoptosis and treating cancer, rheumatoid arthritis, and
ocular disorders comprises a **kininogen** domain 3
analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 57 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and
endothelial cell proliferation, inducing endothelial cell apoptosis and
treating cancer, rheumatoid arthritis, and ocular disorders comprises a
kininogen domain 3 analog -

AB The present sequence is that of an N-terminal fragment of a novel anti-angiogenic D3 peptide (see AAY95414) derived from human high mol.wt.

kininogen (HK) domain 3 (see AAY95426). The full-length D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of peptides of the invention (see AAY95405-26) that are analogues of certain sites in the

HK domain 3. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis, inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95412 Peptide DGENE

TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -

INVENTOR: McCrae R K

PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.

PATENT INFO: WO 2000035407 A2 20000622 44p

APPLICATION INFO: WO 1999-US28465 19991202

PRIORITY INFO: US 1998-112427 19981216

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 58 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -

AB The present sequence is that of a D3 peptide derived from high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide, which may optionally include N-terminal and/or C-terminal protecting groups, **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of peptides of the invention (see AAY95405-26) which are analogues of certain sites in the HK domain 3, in this case amino acids Cys246-Cys249. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including such peptides are used in claimed methods for **inhibiting angiogenesis, inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95411 Peptide DGENE

TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -

INVENTOR: McCrae R K

PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.

PATENT INFO: WO 2000035407 A2 20000622 44p

APPLICATION INFO: WO 1999-US28465 19991202

PRIORITY INFO: US 1998-112427 19981216

DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-42247 [38]

L7 ANSWER 59 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and
endothelial cell proliferation, inducing endothelial cell apoptosis and
treating cancer, rheumatoid arthritis, and ocular disorders comprises a
kininogen domain 3 analog -
AB The present sequence is that of a D3 peptide derived from human high
mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide
inhibits endothelial cell proliferation and thus possesses
anti-angiogenic activity. It is an example of D3 peptides of the
invention (see AAY95405-26) that are analogues of certain sites in the
HK domain 3, in this case amino acid residues Asn275-Lys282. The peptides
inhibit endothelial cell proliferation and may also induce
endothelial cell apoptosis. Compositions including the peptides are
used
in claimed methods for **inhibiting angiogenesis**,
inhibiting endothelial cell proliferation, and inducing
endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular
disorders characterized by undesired vascularization of the retina are
treated. The IC50 value for the present peptide was less than 0.8 uM for
inhibition of fibroblast growth factor-induced HUVEC cell
proliferation.
ACCESSION NUMBER: AAY95410 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis**
and endothelial cell proliferation, inducing endothelial
cell
apoptosis and treating cancer, rheumatoid arthritis, and
ocular disorders comprises a **kininogen** domain 3
analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 60 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and
endothelial cell proliferation, inducing endothelial cell apoptosis and
treating cancer, rheumatoid arthritis, and ocular disorders comprises a
kininogen domain 3 analog -
AB The present sequence is that of a D3 peptide derived from human high
mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide
inhibits endothelial cell proliferation and thus possesses
anti-angiogenic activity. It is an example of D3 peptides of the
invention (see AAY95405-26) that are analogues of certain sites in the
HK domain 3, in this case amino acid residues Asn275-Lys282. The peptides
inhibit endothelial cell proliferation and may also induce
endothelial cell apoptosis. Compositions including the peptides are
used
in claimed methods for **inhibiting angiogenesis**,
inhibiting endothelial cell proliferation, and inducing
endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular
disorders characterized by undesired vascularization of the retina are
treated. The IC50 value for the present peptide was less than 0.8 uM for
inhibition of fibroblast growth factor-induced HUVEC cell

proliferation.

ACCESSION NUMBER: AAY95409 Peptide DGENE

TITLE: Composition for **inhibiting angiogenesis**
and endothelial cell proliferation, inducing endothelial
cell apoptosis and treating cancer, rheumatoid arthritis, and
ocular disorders comprises a **kininogen** domain 3
analog -

INVENTOR: McCrae R K

PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.

PATENT INFO: WO 2000035407 A2 20000622 44p

APPLICATION INFO: WO 1999-US28465 19991202

PRIORITY INFO: US 1998-112427 19981216

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 61 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

TI Composition for **inhibiting angiogenesis** and
endothelial cell proliferation, inducing endothelial cell apoptosis and
treating cancer, rheumatoid arthritis, and ocular disorders comprises a
kininogen domain 3 analog -

AB The present sequence is that of a D3 peptide derived from human high
mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide
inhibits endothelial cell proliferation and thus possesses
anti-angiogenic activity. It is an example of D3 peptides of the
invention (see AAY95405-26) that are analogues of certain sites in the

HK domain 3, in this case amino acid residues Asn275-Lys282. The peptides
inhibit endothelial cell proliferation and may also induce
endothelial cell apoptosis. Compositions including the peptides are
used
in claimed methods for **inhibiting angiogenesis**,
inhibiting endothelial cell proliferation, and inducing
endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular
disorders characterized by undesired vascularization of the retina are
treated.

ACCESSION NUMBER: AAY95408 Peptide DGENE

TITLE: Composition for **inhibiting angiogenesis**
and endothelial cell proliferation, inducing endothelial
cell apoptosis and treating cancer, rheumatoid arthritis, and
ocular disorders comprises a **kininogen** domain 3
analog -

INVENTOR: McCrae R K

PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.

PATENT INFO: WO 2000035407 A2 20000622 44p

APPLICATION INFO: WO 1999-US28465 19991202

PRIORITY INFO: US 1998-112427 19981216

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 62 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

TI Composition for **inhibiting angiogenesis** and
endothelial cell proliferation, inducing endothelial cell apoptosis and
treating cancer, rheumatoid arthritis, and ocular disorders comprises a
kininogen domain 3 analog -

AB The present sequence is that of a C-terminal fragment of a novel
anti-angiogenic D3 peptide (see AAY95408) derived from human high
mol.wt.
kininogen (HK) domain 3 (see AAY95426). The full-length D3

peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of peptides of the invention (see AAY95405-26) that are analogues of certain sites in the

HK domain 3. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis, inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95407 Peptide DGENE
 TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
 INVENTOR: McCrae R K
 PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
 (MCCR-I) MCCRAE R K.
 PATENT INFO: WO 2000035407 A2 20000622 44p
 APPLICATION INFO: WO 1999-US28465 19991202
 PRIORITY INFO: US 1998-112427 19981216
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 63 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
 AB The present sequence is that of an N-terminal fragment of a novel anti-angiogenic D3 peptide (see AAY95408) derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The full-length D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of peptides of the invention (see AAY95405-26) that are analogues of certain sites in the

HK domain 3. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis, inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95406 Peptide DGENE
 TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
 INVENTOR: McCrae R K
 PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
 (MCCR-I) MCCRAE R K.
 PATENT INFO: WO 2000035407 A2 20000622 44p
 APPLICATION INFO: WO 1999-US28465 19991202
 PRIORITY INFO: US 1998-112427 19981216
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 64 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
 AB The present sequence is that of a D3 peptide derived from high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide, which may optionally include N-terminal and/or C-terminal protecting groups, **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of peptides of the invention (see AAY95405-26) which are analogues of certain sites in the HK domain 3, in this case amino acids Asn275-Lys282. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including such peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95405 Peptide DGENE
 TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
 INVENTOR: McCrae R K
 PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
 (MCCR-I) MCCRAE R K.
 PATENT INFO: WO 2000035407 A2 20000622 44p
 APPLICATION INFO: WO 1999-US28465 19991202
 PRIORITY INFO: US 1998-112427 19981216
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 65 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
 TI A pharmaceutical composition used to **inhibit angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
 AB The present sequence is derived from human two-chain high molecular weight **kininogen** (HKa) domain 5. HKa is product of high molecular weight **kininogen** (HK) cleavage by plasma kallikrein. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells. Hka or a synthetic compound comprising the present sequence may be used in a pharmaceutical composition for **inhibiting angiogenesis**. **Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis.
 Peptides used in the composition may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.

ACCESSION NUMBER: AAY81999 peptide DGENE
 TITLE: A pharmaceutical composition used to **inhibit angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -

INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000027866 A1 20000518 52p
APPLICATION INFO: WO 1999-US26419 19991105
PRIORITY INFO: US 1998-107833 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376483 [32]

L7 ANSWER 66 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

TI A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -

AB The present sequence is derived from human two-chain high molecular weight **kininogen** (HKa) domain 5. HKa is product of high molecular weight **kininogen** (HK) cleavage by plasma kallikrein. HK is a 120 kD glycoprotein which binds with high affinity to

endothelial

cells. Hka or a synthetic compound comprising the present sequence may be

used in a pharmaceutical composition for **inhibiting angiogenesis. Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit angiogenesis by inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis.

Peptides used in the composition may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised,

using, for example, solid phase synthesis methods.

ACCESSION NUMBER: AAY81998 peptide DGENE

TITLE: A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -

INVENTOR: McCrae R K

PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.

PATENT INFO: WO 2000027866 A1 20000518 52p

APPLICATION INFO: WO 1999-US26419 19991105

PRIORITY INFO: US 1998-107833 19981110

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2000-376483 [32]

L7 ANSWER 67 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

TI A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -

AB The present sequence is derived from human high molecular weight **kininogen** (HK) domain 5. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells, where it is cleaved to two-chain high molecular weight **kininogen** (HKa) by plasma kallikrein. Hka or a synthetic compound comprising the present sequence may be used in a pharmaceutical composition for **inhibiting angiogenesis. Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit angiogenesis by inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis. Peptides used in the composition may be recombinant peptides,

natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.

ACCESSION NUMBER: AAY81996 peptide DGENE

TITLE: A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -

INVENTOR: McCrae R K

PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.

PATENT INFO: WO 2000027866 A1 20000518 52p

APPLICATION INFO: WO 1999-US26419 19991105

PRIORITY INFO: US 1998-107833 19981110

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2000-376483 [32]

L7 ANSWER 68 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

TI A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -

AB The present sequence is derived from human high molecular weight **kininogen** (HK) domain 5. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells, where it is cleaved to two-chain high molecular weight **kininogen** (HKa) by plasma kallikrein. Hka or a synthetic compound comprising the present sequence may be used in a pharmaceutical composition for **inhibiting angiogenesis**. **Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit angiogenesis by inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis.

Peptides used in the composition may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised,

using, for example, solid phase synthesis methods.

ACCESSION NUMBER: AAY81996 peptide DGENE

TITLE: A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -

INVENTOR: McCrae R K

PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.

PATENT INFO: WO 2000027866 A1 20000518 52p

APPLICATION INFO: WO 1999-US26419 19991105

PRIORITY INFO: US 1998-107833 19981110

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2000-376483 [32]

L7 ANSWER 69 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

TI A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -

AB The present sequence is derived from human high molecular weight **kininogen** (HK) domain 5. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells, where it is cleaved to two-chain high molecular weight **kininogen** (HKa) by plasma kallikrein. Hka or a synthetic compound comprising part or all of the present sequence may be used in a pharmaceutical composition for **inhibiting angiogenesis**. **Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint,

hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis. Peptides used in the composition may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.

ACCESSION NUMBER: AAY81995 peptide DGENE
TITLE: A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000027866 A1 20000518 52p
APPLICATION INFO: WO 1999-US26419 19991105
PRIORITY INFO: US 1998-107833 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376483 [32]

L7 ANSWER 70 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

TI A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -

AB The present sequence is derived from human high molecular weight **kininogen** (HK) domain 5. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells, where it is cleaved to two-chain high molecular weight **kininogen** (HKa) by plasma kallikrein. Hka or a synthetic compound comprising part or all of the present sequence may be used in a pharmaceutical composition for **inhibiting angiogenesis. Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis. Peptides used in the composition may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.

ACCESSION NUMBER: AAY81994 peptide DGENE
TITLE: A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000027866 A1 20000518 52p
APPLICATION INFO: WO 1999-US26419 19991105
PRIORITY INFO: US 1998-107833 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376483 [32]

L7 ANSWER 71 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

TI A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -

AB The present sequence is derived from human high molecular weight **kininogen** (HK) domain 5. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells, where it is cleaved to

two-chain high molecular weight **kininogen** (HKa) by plasma kallikrein. Hka or a synthetic compound comprising part or all of the present sequence may be used in a pharmaceutical composition for **inhibiting angiogenesis**. **Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis. Peptides used in the composition may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.

ACCESSION NUMBER: AAY81993 peptide DGENE
 TITLE: A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
 INVENTOR: McCrae R K
 PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
 (MCCR-I) MCCRAE R K.
 PATENT INFO: WO 2000027866 A1 20000518 52p
 APPLICATION INFO: WO 1999-US26419 19991105
 PRIORITY INFO: US 1998-107833 19981110
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 2000-376483 [32]

L7 ANSWER 72 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

TI A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -

AB The present sequence is derived from human high molecular weight **kininogen** (HK) domain 5. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells, where it is cleaved to two-chain high molecular weight **kininogen** (HKa) by plasma kallikrein. Hka or a synthetic compound comprising part or all of the present sequence may be used in a pharmaceutical composition for **inhibiting angiogenesis**. **Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis. Peptides used in the composition may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.

ACCESSION NUMBER: AAY81992 peptide DGENE
 TITLE: A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
 INVENTOR: McCrae R K
 PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
 (MCCR-I) MCCRAE R K.
 PATENT INFO: WO 2000027866 A1 20000518 52p
 APPLICATION INFO: WO 1999-US26419 19991105
 PRIORITY INFO: US 1998-107833 19981110
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: 2000-376483 [32]

L7 ANSWER 73 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

TI A pharmaceutical composition used to **inhibit**

angiogenesis, inhibit endothelial cell proliferation, and induce endothelial cell apoptosis -

AB The present sequence is derived from human two-chain high molecular weight **kininogen** (HKa) domain 5. HKa is product of high molecular weight **kininogen** (HK) cleavage by plasma kallikrein. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells. Hka or a synthetic compound comprising the present sequence may be used in a pharmaceutical composition for **inhibiting angiogenesis**. **Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit angiogenesis by inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis.

Peptides used in the composition may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.

ACCESSION NUMBER: AAB06337 Protein DGENE

TITLE: A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -

INVENTOR: McCrae R K

PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.

PATENT INFO: WO 2000027866 A1 20000518 52p

APPLICATION INFO: WO 1999-US26419 19991105

PRIORITY INFO: US 1998-107833 19981110

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2000-376483 [32]

L7 ANSWER 74 OF 95 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

TI Role of the light chain of high molecular weight **kininogen** in adhesion, cell-associated proteolysis and **angiogenesis**.

AB Cleavage of high molecular weight **kininogen** (HK) by plasma kallikrein results in a light chain and a heavy chain (HK). The light chain has two domains: D6, which binds (pre)kallikrein, and D5, which binds to anionic surfaces, including heparin as well as zinc. Initially, HK was thought to be important for surface-activated coagulation. HKa or D5 binds to the urokinase receptor on endothelial cells, thereby enhancing the conversion of prourokinase to urokinase by kallikrein, and, thus, cell-associated fibrinolysis. HKa or D5 is antiadhesive by competing with vitronectin binding to the urokinase receptor and/or forming a complex with vitronectin. D5 **inhibits** endothelial cell migration, proliferation, tube formation and **angiogenesis**, thus modulating inflammation and neovascularization.

ACCESSION NUMBER: 2001080473 EMBASE

TITLE: Role of the light chain of high molecular weight **kininogen** in adhesion, cell-associated proteolysis and **angiogenesis**.

AUTHOR: Colman R.W.

CORPORATE SOURCE: R.W. Colman, Sol Sherry Thrombosis Research Ctr., Temple University School of Medicine, Philadelphia, PA 19140, United States

SOURCE: Biological Chemistry, (2001) 382/1 (65-70).

Refs: 22

ISSN: 1431-6730 CODEN: BICHF3

COUNTRY: Germany

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 025 Hematology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

L7 ANSWER 75 OF 95 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

TI IBC's 6th annual conference on **angiogenesis**: Novel therapeutic developments.

AB **Angiogenesis** is a process that is dependent upon co-ordinate production of **angiogenesis** stimulatory and **inhibitory** (angiostatic) molecules. Any imbalance in this regulatory circuit may

lead to the development of a number of **angiogenesis**-mediated diseases. **Angiogenesis** is a multi-step process including activation, adhesion, migration, proliferation and transmigration of endothelial cells across cell matrices to or from new capillaries and from existing vessels. **Angiogenesis** is a process involved in the formation of new vessels by sprouting from pre-existing vessels. In contrast, vessel rudiments are sorted by a process termed vasculogenesis. Endothelial heterogeneity and organ specificity might contribute to differences in the response to different anti-angiogenic mechanisms (cultured EC versus microvascular EC isolated from different tissues). Under normal physiological conditions in mature organisms, endothelial cell turnover or **angiogenesis** is extremely slow (from months to years). However, **angiogenesis** can be activated for a limited time in certain situations such as wound healing and ovulation. In

certain pathological states, such as human metastasis (oncology) and ocular neovascularisation, disorders including diabetic retinopathy and age-related macular degeneration (ophthalmology), there is excessive and sustained **angiogenesis**. Hence, understanding the mechanisms involved in the regulation of **angiogenesis** could have a major impact in the prevention and treatment of pathological angiogenic processes. Additionally, endothelial cells play a major role in the modelling of blood vessels. The interplay of growth factors, cell adhesion molecules, matrix proteases and specific signal transduction pathways either in the maintenance of the quiescent state or in the reactivation of endothelial cells is critical in physiological and pathological angiogenic processes.

ACCESSION NUMBER: 2001050805 EMBASE

TITLE: IBC's 6th annual conference on **angiogenesis**:
Novel therapeutic developments.

AUTHOR: Mousa S.A.

CORPORATE SOURCE: S.A. Mousa, DuPont Pharmaceuticals Co., Wilmington, DE,
United States

SOURCE: Expert Opinion on Investigational Drugs, (2001) 10/2
(387-391).

ISSN: 1354-3784 CODEN: EOIDER

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 005 General Pathology and Pathological Anatomy
012 Ophthalmology
014 Radiology
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

L7 ANSWER 76 OF 95 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

TI Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits angiogenesis**: Partial activity within domain 5.
AB We previously reported that the binding of two-chain high molecular weight

kininogen (HKa) to endothelial cells may occur through interactions with endothelial urokinase receptors. Since the binding of urokinase to urokinase receptors activates signaling responses and may stimulate mitogenesis, we assessed the effect of HKa binding on endothelial cell proliferation. Unexpectedly, HKa **inhibited** proliferation in response to several growth factors, with 50% **inhibition** caused by .apprx.10 nM HKa. This activity was Zn²⁺ dependent and not shared by either single-chain high molecular weight **kininogen** (HK) or low molecular weight **kininogen**. HKa selectively **inhibited** the proliferation of human umbilical vein and dermal microvascular endothelial cells, but did not affect that of umbilical vein or human aortic smooth muscle cells, trophoblasts, fibroblasts, or carcinoma cells. **Inhibition** of endothelial proliferation by HKa was associated with endothelial cell apoptosis and unaffected by antibodies that block the binding of HK or HKa to any of their known endothelial receptors. Recombinant HK domain 5 displayed activity similar to that of HKa. In vivo, HKa **inhibited** neovascularization of subcutaneously implanted Matrigel plugs, as well as rat corneal **angiogenesis**. These results demonstrate that HKa is a novel **inhibitor** of **angiogenesis**, whose activity is dependent on the unique conformation of the two-chain molecule.

ACCESSION NUMBER: 2000436640 EMBASE
TITLE: Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits angiogenesis**: Partial activity within domain 5.
AUTHOR: Zhang J.-C.; Claffey K.; Sakthivel R.; Darzynkiewicz Z.; Shaw D.E.; Leal J.; Wang Y.-C.; Lu F.-M.; McCrae K.R.
CORPORATE SOURCE: K.R. McCrae, Hematology-Oncology Division, Case Western Reserve University, School of Medicine, 10900 Euclid Ave., Cleveland, OH 44106-4937, United States. kxm71@po.cwru.edu
SOURCE: FASEB Journal, (2000) 14/15 (2589-2600).
Refs: 69
ISSN: 0892-6638 CODEN: FAJOEC
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

L7 ANSWER 77 OF 95 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

TI The hemostatic system as a regulator of **angiogenesis**.

ACCESSION NUMBER: 2000041562 EMBASE
TITLE: The hemostatic system as a regulator of **angiogenesis**.
AUTHOR: Browder T.; Folkman J.; Pirie-Shepherd S.
CORPORATE SOURCE: J. Folkman, Children's Hospital, Hunnewell 103, 300 Longwood Ave., Boston, MA 02115, United States
SOURCE: Journal of Biological Chemistry, (21 Jan 2000) 275/3 (1521-1524).
Refs: 67
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 025 Hematology
029 Clinical Biochemistry
LANGUAGE: English

L7 ANSWER 78 OF 95 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

TI Domain 5 of high molecular weight **kininogen** (kininostatin) down-

regulates endothelial cell proliferation and migration and **inhibits angiogenesis**.

AB We have demonstrated that high molecular weight **kininogen** (HK) binds specifically on endothelial cells to domain 2/3 of the urokinase receptor (uPAR). **Inhibition** by vitronectin suggests that kallikrein-cleaved HK (HKa) is antiadhesive. Plasma kallikrein bound to

HK

cleaves prourokinase to urokinase, initiating cell-associated fibrinolysis. We postulated that HK cell binding domains would **inhibit angiogenesis**. We found that recombinant domain 5 (D5) **inhibited** endothelial cell migration toward vitronectin 85% at 0.27 μ M with an IC₅₀ (concentration to yield 50% **inhibition**) = 0.12 μ M. A D5 peptide, G486-K502, showed an IC₅₀ = 0.2 μ M, but a 25-mer peptide from a D3 cell binding domain only **inhibited** migration 10% at 139 μ M (IC₅₀ > 50 μ M). D6 exhibited weaker **inhibitory** activity (IC₅₀ = 0.50 μ M). D5 also potently **inhibited** endothelial cell proliferation with an IC₅₀ = 30 nM, while D3 and D6 were inactive. Using deletion mutants of D5, we localized the smallest region for full activity to H441-D474. To further map the active region, we created a molecular homology model of D5 and designed a series of peptides displaying surface loops. Peptide 440-455 was the most potent (IC₅₀ = 100 nM) in **inhibiting** proliferation but did not **inhibit** migration. D5 **inhibited angiogenesis** stimulated by fibroblast growth factor FGF2 (97%) in a chicken chorioallantoic membrane assay at 270 nM, and peptide 400-455 was also **inhibitory** (79%). HK D5 (for which we suggest the designation, 'kininostatin') is a potent **inhibitor** of endothelial cell migration and proliferation in vitro and of **angiogenesis** in vivo.

ACCESSION NUMBER: 2000028682 EMBASE

TITLE: Domain 5 of high molecular weight **kininogen** (kininostatin) down- regulates endothelial cell proliferation and migration and **inhibits angiogenesis**.

AUTHOR: Colman R.W.; Jameson B.A.; Lin Y.; Johnson D.; Mousa S.A.

CORPORATE SOURCE: R.W. Colman, Sol Sherry Thrombosis Res. Center, Temple University School of Medicine, 3400 North Broad St, Philadelphia, PA 19140, United States.
colmanr@astro.temple.edu

SOURCE: Blood, (15 Jan 2000) 95/2 (543-550).

Refs: 52

ISSN: 0006-4971 CODEN: BLOOAW

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 025 Hematology

029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

L7 ANSWER 79 OF 95 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

TI Biologic activities of the contact factors in vivo. Potentiation of hypotension, inflammation, and fibrinolysis, and **inhibition** of cell adhesion, **angiogenesis** and thrombosis.

ACCESSION NUMBER: 1999423254 EMBASE

TITLE: Biologic activities of the contact factors in vivo. Potentiation of hypotension, inflammation, and fibrinolysis, and **inhibition** of cell adhesion, **angiogenesis** and thrombosis.

AUTHOR: Colman R.W.

CORPORATE SOURCE: Dr. R.W. Colman, Sol Sherry Thrombosis Res. Center, Temple University School of Medicine, 3400 North Broad Street, Philadelphia, PA 19140, United States.
colmanr@astro.temple.edu

SOURCE: Thrombosis and Haemostasis, (1999) 82/6 (1568-1577).

Refs: 127
 ISSN: 0340-6245 CODEN: THHADQ
 COUNTRY: Germany
 DOCUMENT TYPE: Journal; General Review
 FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
 025 Hematology
 037 Drug Literature Index
 LANGUAGE: English

L7 ANSWER 80 OF 95 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

TI Kallikrein-kinin in infection and cancer.

AB This review article describes the mechanism of enhancement of vascular permeability in infectious disease and cancer. This phenomenon is primarily mediated by bradykinin, nitric oxide and other unique vascular mediators. They are highly intermingled with each other in these disease states. Furthermore, these mediators are elicited in various in vivo settings most frequently induced by bacterial proteases, and indirect or direct activation of kallikrein-kinin cascade at one or more steps. The key steps involve bacterial proteases or cellular components including lipopolysaccharides. Thus, the use of appropriate protease inhibitors or antagonists, or scavengers in the case of nitric oxide, superoxide or peroxynitrite, are anticipated to attenuate the clinical manifestation induced by such mediators. It also explained that fluid accumulation in ascitic or pleural compartments in the case of carcinomatosis in terminal cancer patients can be largely attributed to bradykinin or related mechanism. Systemic bacterial dissemination is also facilitated by bradykinin, or suppressed by kinin antagonists as well as by the inhibition of kinin production, respectively. Thus, control of the level of such vascular mediators appears important both in infectious disease and in cancer. .alpha.1-Protease inhibitor, which inhibits neutrophil elastase, is inactivated by oxidative metabolites such as superoxide and peroxynitrite, and this effect activates matrix metalloproteinases. This indicates that oxidative stress activates proteolytic potential, and thus accelerates the degenerative process upon infection. Copyright (C) 1999 Elsevier Science B.V.

ACCESSION NUMBER: 1999415976 EMBASE

TITLE: Kallikrein-kinin in infection and cancer.

AUTHOR: Maeda H.; Wu J.; Okamoto T.; Maruo K.; Akaike T.

CORPORATE SOURCE: H. Maeda, Department of Microbiology, Kumamoto University, School of Medicine, Honjo 2-2-1, Kumamoto 860-0811, Japan.
 msmaedah@gpo.kumamoto-u.ac.jp

SOURCE: Immunopharmacology, (1999) 43/2-3 (115-128).
 Refs: 47

ISSN: 0162-3109 CODEN: IMMUDP
 S 0162-3109(99)00104-6

PUBLISHER IDENT.:

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 016 Cancer
 018 Cardiovascular Diseases and Cardiovascular Surgery
 037 Drug Literature Index
 004 Microbiology
 005 General Pathology and Pathological Anatomy

LANGUAGE: English

SUMMARY LANGUAGE: English

L7 ANSWER 81 OF 95 SCISEARCH COPYRIGHT 2001 ISI (R)

TI Role of the light chain of high molecular weight **kininogen** in adhesion, cell-associated proteolysis and **angiogenesis**

AB Cleavage of high molecular weight **kininogen** (HK) by plasma kallikrein results in a light chain and a heavy chain (HK). The light chain has two domains: D6, which binds (pre)kallikrein, and D5, which binds to anionic surfaces, including heparin as well as zinc. Initially, HK was thought to be important for surface-activated coagulation. HKa or D5 binds to the urokinase receptor on endothelial cells, thereby enhancing

the conversion of prourokinase to urokinase by kallikrein, and, thus, cell-associated fibrinolysis. HKa or D5 is antiadhesive by competing with vitronectin binding to the urokinase receptor and for forming a complex with vitronectin. D5 **inhibits** endothelial cell migration, proliferation, tube formation and **angiogenesis**, thus modulating inflammation and neovascularization.

ACCESSION NUMBER: 2001:193846 SCISEARCH

THE GENUINE ARTICLE: 406YE

TITLE: Role of the light chain of high molecular weight **kininogen** in adhesion, cell-associated proteolysis and **angiogenesis**

AUTHOR: Colman R W (Reprint)

CORPORATE SOURCE: Temple Univ, Sch Med, Sol Sherry Thrombosis Res Ctr, Philadelphia, PA 19140 USA (Reprint)

COUNTRY OF AUTHOR: USA

SOURCE: BIOLOGICAL CHEMISTRY, (JAN 2001) Vol. 382, No. 1, pp. 65-70.

Publisher: WALTER DE GRUYTER & CO, GENTHINER STRASSE 13, D-10785 BERLIN, GERMANY.

ISSN: 1431-6730.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 22

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L7 ANSWER 82 OF 95 SCISEARCH COPYRIGHT 2001 ISI (R)

TI Patent focus on cancer chemotherapeutics. II **angiogenesis** agents: April 2000-September 2000

AB **Angiogenesis** refers to the formation of capillary blood vessels from existing blood vessels: a process that is believed to be critical for tumour growth and metastasis. **Angiogenesis inhibition** represents a new approach to cancer chemotherapy with several agents and approaches non; entering late clinical development. This review summarises the key aspects of recent patent applications referring to **inhibitors of angiogenesis** that have been published between April and September 2000. The review covers the main mechanism-based approaches such as MMPI, integrin antagonists, urokinase **inhibitors** and **inhibitors** of the growth factor signalling pathways of fibroblast growth factor (FGF), platelet derived growth factor (PDGF), vascular endothelial growth factor (VEGF) and Tie-2/Tek. Applications referring to endogenous **inhibitors** such as endostatin or angiostatin are also included, as are selected natural products that have data suggesting a link to **angiogenesis** -specific mechanisms of action.

ACCESSION NUMBER: 2001:117935 SCISEARCH

THE GENUINE ARTICLE: 396EC

TITLE: Patent focus on cancer chemotherapeutics. II **angiogenesis** agents: April 2000-September 2000

AUTHOR: Connell R D (Reprint); Beebe J S

CORPORATE SOURCE: Pfizer Corp, Canc Drug Discovery, MS 8118W-B2, Eastern Point Rd, Groton, CT 06340 USA (Reprint); Pfizer Corp, Canc Drug Discovery, Groton, CT 06340 USA

COUNTRY OF AUTHOR: USA

SOURCE: EXPERT OPINION ON THERAPEUTIC PATENTS, (JAN 2001) Vol. 11,

No. 1, pp. 77-114.

Publisher: ASHLEY PUBLICATIONS LTD, UNITEC HOUSE, 3RD FL, 2 ALBERT PLACE FINCHLEY CENTRAL, LONDON N3 1QB, ENGLAND.

ISSN: 1354-3776.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 58

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L7 ANSWER 83 OF 95 SCISEARCH COPYRIGHT 2001 ISI (R)

TI Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits angiogenesis**: partial activity within domain 5

AB We previously reported that the binding of two-chain high molecular weight **kininogen** (HKa) to endothelial cells may occur through interactions with endothelial urokinase receptors. Since the binding of urokinase to urokinase receptors activates signaling responses and may stimulate mitogenesis, we assessed the effect of HKa binding on endothelial cell proliferation. Unexpectedly, HKa **inhibited** proliferation in response to several growth factors, with 50% **inhibition** caused by similar to 10 nM HKa. This activity was Zn²⁺ dependent and not shared by either single-chain high molecular weight **kininogen** (HK) or low molecular weight **kininogen**. HKa selectively **inhibited** the proliferation of human umbilical vein and dermal microvascular endothelial cells, but did not affect that of umbilical vein or human aortic smooth muscle cells, trophoblasts, fibroblasts, or carcinoma cells. **Inhibition** of endothelial proliferation by HKa was associated with endothelial cell apoptosis and unaffected by antibodies that block the binding of HK or HKa to any of their known endothelial receptors. Recombinant HK domain 5 displayed activity similar to that of HKa. In vivo, HKa **inhibited** neovascularization of subcutaneously implanted Matrigel plugs, as well as rat corneal **angiogenesis**. These results demonstrate that HKa is a novel **inhibitor** of **angiogenesis**, whose activity is dependent on the unique conformation of the two-chain molecule.

ACCESSION NUMBER: 2000:939227 SCISEARCH

THE GENUINE ARTICLE: 380VD

TITLE: Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits angiogenesis**: partial activity within domain 5

AUTHOR: Zhang J C; Claffey K; Sakthivel R; Darzynkiewicz Z; Shaw D

CORPORATE SOURCE: E; Leal J; Wang Y C; Lu F M; McCrae K R (Reprint)
CASE WESTERN RESERVE UNIV, SCH MED, DIV HEMATOL ONCOL, BRB

3, 10900 EUCLID AVE, CLEVELAND, OH 44106 (Reprint); CASE WESTERN RESERVE UNIV, SCH MED, DIV HEMATOL ONCOL, CLEVELAND, OH 44106; CASE WESTERN RESERVE UNIV, SCH MED, DEPT MED, CLEVELAND, OH 44106; UNIV CONNECTICUT, SCH MED, CTR VASC BIOL, DEPT PHYSIOL, FARMINGTON, CT; NEW YORK MED COLL, VALHALLA, NY 10595; DE SHAW & CO INC, NEW YORK, NY; ATTENUON LLC, SAN DIEGO, CA; ABBOTT LABS, DIV PHARMACEUT PROD, DEPT CHEMOTHERAPEUT, ABBOTT PK, IL 60064; ALLEGHENY UNIV HLTH SCI, CTR NEUROVIROL & NEUROONCOL, PHILADELPHIA, PA 19102

COUNTRY OF AUTHOR: USA

SOURCE: FASEB JOURNAL, (DEC 2000) Vol. 14, No. 15, pp. 2589-2600.

Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998.

ISSN: 0892-6638.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: English

REFERENCE COUNT: 69

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L7 ANSWER 84 OF 95 SCISEARCH COPYRIGHT 2001 ISI (R)

TI **Inhibition** of **angiogenesis** by peptides derived from **kininogen** domain 5 & by a monoclonal antibody to **kininogen** domain 5

ACCESSION NUMBER: 2000:150003 SCISEARCH

THE GENUINE ARTICLE: 282GL

TITLE: **Inhibition of angiogenesis** by peptides derived from **kininogen** domain 5 & h...
 AUTHOR: Mousa S A (Reprint); Mohamed S; Powell J; Colman R W
 CORPORATE SOURCE: DUPONT PHARMACEUT, WILMINGTON, DE; TEMPLE UNIV, SCH MED, SOL SHERRY THROMBOSIS RES CTR, PHILADELPHIA, PA
 COUNTRY OF AUTHOR: USA
 SOURCE: JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY, (FEB 2000)
 Vol. 35, No. 2, Supp. [A], pp. A295-A296.
 Publisher: ELSEVIER SCIENCE INC, 655 AVENUE OF THE AMERICAS, NEW YORK, NY 10010.
 ISSN: 0735-1097.
 DOCUMENT TYPE: Conference; Journal
 FILE SEGMENT: LIFE; CLIN
 LANGUAGE: English
 REFERENCE COUNT: 0

L7 ANSWER 85 OF 95 SCISEARCH COPYRIGHT 2001 ISI (R)
 TI **Inhibition of angiogenesis** by two-chain high molecular weight **kininogen** (HKa) is associated with induction of endothelial cell apoptosis.

ACCESSION NUMBER: 2000:51161 SCISEARCH

THE GENUINE ARTICLE: 257PH

TITLE: **Inhibition of angiogenesis** by two-chain high molecular weight **kininogen** (HKa) is associated with induction of endothelial cell apoptosis.

AUTHOR: Zhang J C (Reprint); Sakthivel R; Lu F M; Darzynkiewicz Z;

CORPORATE SOURCE: McCrae K R
 CASE WESTERN RESERVE UNIV, SCH MED, CLEVELAND, OH; ALLEGHENY UNIV HLTH SCI, CTR NEUROVIROL & NEUROONCOL, PHILADELPHIA, PA 19102; NEW YORK MED COLL, VALHALLA, NY 10595

COUNTRY OF AUTHOR: USA

SOURCE: BLOOD, (15 NOV 1999) Vol. 94, No. 10, Part 1, Supp. [1], pp. 36-36.

Publisher: AMER SOC HEMATOLOGY, 1200 19TH ST, NW, STE

300,

WASHINGTON, DC 20036-2422.

ISSN: 0006-4971.

DOCUMENT TYPE: Conference; Journal

FILE SEGMENT: LIFE; CLIN

LANGUAGE: English

REFERENCE COUNT: 0

L7 ANSWER 86 OF 95 SCISEARCH COPYRIGHT 2001 ISI (R)

TI Two chain high molecular weight **kininogen** **inhibits** endothelial cell proliferation and **angiogenesis**: Partial activity within domain

ACCESSION NUMBER: 2000:51156 SCISEARCH

THE GENUINE ARTICLE: 257PH

TITLE: Two chain high molecular weight **kininogen** **inhibits** endothelial cell proliferation and **angiogenesis**: Partial activity within domain

AUTHOR: Zhang J C (Reprint); Claffey K P; Sakthivel R; Leal J; McCrae K R

CORPORATE SOURCE: CASE WESTERN RESERVE UNIV, SCH MED, CLEVELAND, OH; UNIV CONNECTICUT, SCH MED, FARMINGTON, CT; ABBOTT LABS, ABBOTT PK, IL 60064

COUNTRY OF AUTHOR: USA

SOURCE: BLOOD, (15 NOV 1999) Vol. 94, No. 10, Part 1, Supp. [1], pp. 31-31.

300,

Publisher: AMER SOC HEMATOLOGY, 1200 19TH ST, NW, STE

WASHINGTON, DC 20036-2422.

ISSN: 0006-4971.

DOCUMENT TYPE:

Conference; Journal

FILE SEGMENT:

LIFE; CLIN

LANGUAGE:

English

REFERENCE COUNT:

0

L7 ANSWER 87 OF 95 SCISEARCH COPYRIGHT 2001 ISI (R)

TI **Inhibition** of tumor **angiogenesis** by a monoclonal antibody to **kininogen** domain

ACCESSION NUMBER: 2000:51154 SCISEARCH

THE GENUINE ARTICLE: 257PH

TITLE:

Inhibition of tumor **angiogenesis** by a monoclonal antibody to **kininogen** domain

AUTHOR:

Colman R W (Reprint); Mousa S A

CORPORATE SOURCE:

TEMPLE UNIV, SOL SHERRY THROMBOSIS RES CTR, SCH MED, PHILADELPHIA, PA 19122; DUPONT PHARMACEUT, WILMINGTON, DE

COUNTRY OF AUTHOR:

USA

SOURCE:

BLOOD, (15 NOV 1999) Vol. 94, No. 10, Part 1, Supp. [1], pp. 29-29.

Publisher: AMER SOC HEMATOLOGY, 1200 19TH ST, NW, STE

300,

WASHINGTON, DC 20036-2422.

ISSN: 0006-4971.

DOCUMENT TYPE:

Conference; Journal

FILE SEGMENT:

LIFE; CLIN

LANGUAGE:

English

REFERENCE COUNT:

0

L7 ANSWER 88 OF 95 SCISEARCH COPYRIGHT 2001 ISI (R)

TI Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and **inhibits angiogenesis**

AB We have demonstrated that high molecular weight **kininogen** (HK) binds specifically on endothelial cells to domain 2/3 of the urokinase receptor (uPAR). **Inhibition** by vitronectin suggests that kallikrein-cleaved HK (HKa) is antiadhesive. Plasma kallikrein bound to HK cleaves prourokinase to urokinase, initiating cell-associated fibrinolysis. We postulated that HK cell binding domains would **inhibit angiogenesis**. We found that recombinant domain 5 (D5) **inhibited** endothelial cell migration toward vitronectin 85% at 0.27 μ M with an IC₅₀ (concentration to yield 50% **inhibition**) = 0.12 μ M. A D5 peptide, G486-K502, showed an IC₅₀ = 0.2 μ M, but a 25-mer peptide from a D3 cell binding domain only **inhibited** migration 10% at 139 μ M (IC₅₀ > 50 μ M). D6 exhibited weaker **inhibitory** activity (IC₅₀ = 0.50 μ M). D5 also potently **inhibited** endothelial cell proliferation with an IC₅₀ = 30 nM, while D3 and D6 were inactive. Using deletion mutants of D5, we localized the smallest region for full activity to H441-D474. To further map the active region, we created a molecular homology model of D5 and designed a series of peptides displaying surface loops. Peptide 440-155 was the most potent (IC₅₀ = 100 nM) in **inhibiting** proliferation but did not **inhibit** migration. D5 **inhibited angiogenesis** stimulated by fibroblast growth factor FGF2 (97%) in a chicken chorioallantoic membrane assay at 270 nM, and peptide 400-455 was also **inhibitory** (79%), HK D5 (for which we suggest the designation, 'kininostatin') is a potent **inhibitor** of endothelial cell migration and proliferation in vitro and of **angiogenesis** in vivo. (Blood, 2000;95:543-550) (C) 2000 by The American Society of Hematology.

ACCESSION NUMBER: 2000:48248 SCISEARCH

THE GENUINE ARTICLE: 272QG

TITLE: Domain 5 of high molecular weight **kininogen**
(kininostatin) down-regulates endothelial cell
proliferation and migration and **inhibits**
angiogenesis

AUTHOR: Colman R W (Reprint); Jameson B A; Lin Y Z; Johnson D;
Mousa S A

CORPORATE SOURCE: TEMPLE UNIV, SOL SHERRY THROMBOSIS RES CTR, SCH MED, 3400
N BROAD ST, PHILADELPHIA, PA 19140 (Reprint); MCP
HAHNEMANN MED SCH, CTR NEUROVIROL, PHILADELPHIA, PA;
DUPONT MERCK PHARMACEUT CO, DIV CARDIOVASC, WILMINGTON,
DE 19880

COUNTRY OF AUTHOR: USA

SOURCE: BLOOD, (15 JAN 2000) Vol. 95, No. 2, pp. 543-550.
Publisher: AMER SOC HEMATOLOGY, 1200 19TH ST, NW, STE
300,
WASHINGTON, DC 20036-2422.
ISSN: 0006-4971.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE; CLIN

LANGUAGE: English

REFERENCE COUNT: 51

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L7 ANSWER 89 OF 95 SCISEARCH COPYRIGHT 2001 ISI (R)

TI Biologic activities of the contact factors in vivo - Potentiation of
hypotension, inflammation, and fibrinolysis, and **inhibition** of
cell adhesion, **angiogenesis** and thrombosis

ACCESSION NUMBER: 1999:971544 SCISEARCH

THE GENUINE ARTICLE: 264UN

TITLE: Biologic activities of the contact factors in vivo -
Potentiation of hypotension, inflammation, and
fibrinolysis, and **inhibition** of cell adhesion,
angiogenesis and thrombosis

AUTHOR: Colman R W (Reprint)

CORPORATE SOURCE: TEMPLE UNIV, SCH MED, SOL SHERRY THROMBOSIS RES CTR, 3400
N BROAD ST, PHILADELPHIA, PA 19140 (Reprint)

COUNTRY OF AUTHOR: USA

SOURCE: THROMBOSIS AND HAEMOSTASIS, (DEC 1999) Vol. 82, No. 6,
PP. 1568-1577.
Publisher: F K SCHATTAUER VERLAG GMBH, P O BOX 10 45 43,
LENZHALDE 3, D-70040 STUTTGART, GERMANY.
ISSN: 0340-6245.

DOCUMENT TYPE: General Review; Journal

FILE SEGMENT: LIFE

LANGUAGE: English

REFERENCE COUNT: 126

L7 ANSWER 90 OF 95 SCISEARCH COPYRIGHT 2001 ISI (R)

TI Domain 5 of high molecular weight **kininogen** (kininostatin)
downregulates endothelial cell proliferation and migration and
inhibits angiogenesis.

ACCESSION NUMBER: 1999:763940 SCISEARCH

THE GENUINE ARTICLE: 226QX

TITLE: Domain 5 of high molecular weight **kininogen**
(kininostatin) downregulates endothelial cell
proliferation and migration and **inhibits**
angiogenesis.

AUTHOR: Colman R W (Reprint); Jameson B; Mousa S A

CORPORATE SOURCE: TEMPLE UNIV, SCH MED, SOL SHERRY THROMBOSIS RES CTR,
PHILADELPHIA, PA 19122; DUPONT MERCK PHARMACEUT CO,
WILMINGTON, DE 19880; ALLEGHENY UNIV HLTH SCI,
PHILADELPHIA, PA 19102

COUNTRY OF AUTHOR: USA
SOURCE: FASEB JOURNAL, (23 APR 1999) Vol. No. 7, Supp. [S],
pp. A1407-A1407.
Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE
PIKE, BETHESDA, MD 20814-3998.
ISSN: 0892-6638.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 0

L7 ANSWER 91 OF 95 SCISEARCH COPYRIGHT 2001 ISI (R)
TI **Inhibition of angiogenesis** by peptides derived from
kininogen.

ACCESSION NUMBER: 1999:1270 SCISEARCH
THE GENUINE ARTICLE: 141AW
TITLE: **Inhibition of angiogenesis** by peptides
derived from **kininogen**.
AUTHOR: Colman R W (Reprint); Lin Y; Johnson D; Mousa S A
CORPORATE SOURCE: DUPONT MERCK PHARMACEUT CO, WILMINGTON, DE 19880; TEMPLE
UNIV, SCH MED, SOL SHERRY THROMBOSIS RES CTR,
PHILADELPHIA, PA 19122

COUNTRY OF AUTHOR: USA
SOURCE: BLOOD, (15 NOV 1998) Vol. 92, No. 10, Part 1, Supp. [1],
pp. 701-701.
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST
CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399.
ISSN: 0006-4971.

DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L7 ANSWER 92 OF 95 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

TI **Inhibiting angiogenesis** in a mammal using an antibody
against high molecular weight **kininogen** domain 5.

AN 2001-328940 [34] WPIDS

AB WO 200134195 A UPAB: 20010620

NOVELTY - **Inhibiting angiogenesis** or tumor growth or
formation in a mammal, comprising administering an antibody (Ab1) against
an antigenic determinant of high molecular weight **kininogen**
domain 5 (HMWKd5), is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for
inhibiting endothelial cell proliferation, comprising contacting
endothelial cells with Ab1.

ACTIVITY - Cytostatic; antidiabetic; ophthalmological;
antirheumatic;
antiarthritic; antiatherosclerotic.

A chicken chorioallantoic neovascularization assay was performed to
determine the **inhibition of angiogenesis** by antibody
MabC11C1, the product of hybridoma ATCC HB-8964. In 10 day old chicken
embryos a small hole was made in the shell concealing the air sac and a
second hole directly over an avascular portion of the embryonic membrane.
A false air sac was created beneath the second hole using negative
pressure to the first hole which caused the chorioallantoic membrane
(CAM)

to separate from the shell. A 1 cm² window was cut in to the shell over
the dropped CAM and sterilized Whatman number 1 filter disks adsorbed
with

fibroblast growth factor (FGF)-2 (Life technologies) in phosphate
buffered

saline (PBS) at 1 micro g/ml were placed on the growing CAMs. A range of
Mab concentrations in 25 micro liter buffered saline was applied to the
saturated filter 24 hours later. CAM tissue beneath the filter was

resected from embryos 48 hours post treatment. Sections were examined under a SV6 stereo microscope at 50x magnification. The number of vessel branch points contained in a circular region equal to the area of a filter

disk was counted for each section. Results showed that MabC11C1 **inhibited** the FGF-2 stimulated neovascularization by 71.3%.

MECHANISM OF ACTION - Antibody therapy.

USE - The invention is used to **inhibit** endothelial cell proliferation, vascular tube formation and/or neovascularization in disease states such as diabetic retinopathy, rheumatoid arthritis and atherosclerotic plaques and during tumor growth.

Dwg.0/8

ACCESSION NUMBER: 2001-328940 [34] WPIDS
DOC. NO. CPI: C2001-100961
TITLE: **Inhibiting angiogenesis** in a mammal
using an antibody against high molecular weight
kininogen domain 5.
DERWENT CLASS: B04 D16
INVENTOR(S): COLMAN, R W; MOUSA, S A
PATENT ASSIGNEE(S): (DUPO) DUPONT PHARM CO; (UTEM) UNIV TEMPLE
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG																		
WO 2001034195	A1	20010517	(200134)*	EN	19																		
RW:	AT	BE	CH	CY	DE	DK	EA	ES	FI	FR	GB	GH	GM	GR	IE	IT	KE	LS	LU	MC	MW	MZ	
	NL	OA	PT	SD	SE	SL	SZ	TR	TZ	UG	ZW												
W:	AE	AG	AL	AM	AT	AU	AZ	BA	BB	BG	BR	BY	BZ	CA	CH	CN	CR	CU	CZ	DE	DK	DM	
	DZ	EE	ES	FI	GB	GD	GE	GH	GM	HR	HU	ID	IL	IN	IS	JP	KE	KG	KP	KR	KZ	LC	
	LK	LR	LS	LT	LU	LV	MA	MD	MG	MK	MN	MW	MX	MZ	NO	NZ	PL	PT	RO	RU	SD	SE	
	SG	SI	SK	SL	TJ	TM	TR	TT	TZ	UA	UG	US	UZ	VN	YU	ZA	ZW						

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001034195	A1	WO 2000-US30975	20001110

PRIORITY APPLN. INFO: US 1999-165165 19991112

L7 ANSWER 93 OF 95 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Treating vascularized tumors using constructs comprising angiopoietins which bind to stably-expressed aminophospholipids of tumor blood vessels.
AN 2001-081048 [09] WPIDS
AB WO 200103735 A UPAB: 20010213
NOVELTY - Therapeutic constructs and conjugates that bind to aminophospholipids and contain angiopoietins, and methods of delivering those angiopoietins to stably-expressed aminophospholipids of tumor blood vessels for the treatment of cancer (e.g. vascularized tumors), are new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:
(1) a binding ligand (I) comprising a targeting agent that binds to an aminophospholipid operatively attached to an angiopoietin;
(2) an antibody construct (II), comprising an anti-aminophospholipid antibody or antigen binding fragment operatively attached to an angiopoietin;
(3) a kit (III) comprising a targeting agent -angiopoietin construct that comprises a targeting agent that binds to an aminophospholipid operatively attached to an angiopoietin and:
(a) a targeting agent-detectable agent construct that comprises a second targeting agent that binds to an aminophospholipid operatively attached to a detectable agent; and/or

(b) a second anticancer agent;
(4) a method (IV) for treating an animal having a vascularized tumor,

comprising administering a binding ligand that comprises an angiopoietin operatively attached to a targeting agent that binds to an aminophospholipid on the luminal surface of blood vessels of a vascularized tumor;

(5) a method (V) for inducing tumor regression, comprising administering to an animal (which has a vascularized tumor), a binding ligand that induces regression in the tumor blood vessels (the binding ligand comprises angiopoietin-2 operatively attached to a targeting agent that binds to an aminophospholipid expressed on the luminal surface of blood vessels of the vascularized tumor); and

(6) a method (VI) for **inhibiting** tumor growth, comprising administering to an animal (which has a vascularized tumor), a binding ligand that **inhibits** the growth of the tumor blood vessels (the binding ligand comprises angiopoietin-1 operatively attached to a targeting agent that binds to an aminophospholipid expressed on the luminal surface of blood vessels of the vascularized tumor).

ACTIVITY - Cytostatic.

Male CB17 SCID (severely combined immunodeficiency) mice were injected subcutaneously with 1 multiply 107 L540 tumor cells. When the tumors had reached a volume of 0.4-0.6 cm³, the mice were injected intravenously with either 4 micro g tTF (truncated tissue factor), 20 micro g of anti-VCAM-1.tTF, 16 micro g anti-VCAM-1 antibody, a mixture of 6 micro g of anti-VCAM-1 antibody and 4 micro g of tTF, 20 micro g control

IgG.tTF or saline.

Mice were sacrificed when tumors reached a volume of 2 cm³ (or earlier if they showed necrosis or ulceration).

Mean tumor volume of anti-VCAM-1.tTF treated mice was significantly reduced after 21 days of treatment in comparison to all other groups.

Nine

out of 15 mice treated with the specific coaguligand showed more than 50% reduction in tumor volume. The effect was specific as un-conjugated tTF, control IgG coaguligand and mixtures of free anti-VCAM-1 antibody and tTF did not affect tumor growth.

MECHANISM OF ACTION - **Inhibition** of tumor angiogenesis.

USE - The constructs, conjugates and methods ((I)-(VI)) may be used for the treatment of cancers, especially vascularized tumors, and for preventing **angiogenesis** within cancerous tissue.

Dwg.0/4

ACCESSION NUMBER: 2001-081048 [09] WPIDS
DOC. NO. CPI: C2001-023403
TITLE: Treating vascularized tumors using constructs comprising angiopoietins which bind to stably-expressed aminophospholipids of tumor blood vessels.
DERWENT CLASS: B04 D16
INVENTOR(S): THORPE, P E
PATENT ASSIGNEE(S): (MAIN-N) MAINE MEDICAL CENT RES INST; (TEXA) UNIV TEXAS SYSTEM
COUNTRY COUNT: 22
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001003735	A1	20010118	(200109)*	EN	245
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU CA JP US					
AU 2000062081	A	20010130	(200127)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001003735	A1	WO 2000-US18779	20000711
AU 2000062081	A	AU 2000-62081	20000711

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000062081	A	WO 200103735

PRIORITY APPLN. INFO: US 1999-143762 19990712

L7 ANSWER 94 OF 95 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
 TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog.
 AN 2000-442247 [38] WPIDS
 AB WO 200035407 A UPAB: 20000811
 NOVELTY - A pharmaceutical composition comprising a compound of 8 to 32 amino acids (A) that is a **kininogen** domain 3 analog and optionally contains an amino-terminal and/or carboxy-terminal protecting group.

DETAILED DESCRIPTION - The pharmaceutical composition comprises a compound with the formula X1 Asn Asn Ala Thr Phe Tyr Phe Lys X2, (A) where

X1 and X2 are from zero to twelve amino acids.

INDEPENDENT CLAIMS are also included for the following:

(1) A pharmaceutical composition comprising a compound with the formula X3 Cys Val Gly Cys X4 (B), where X3 and X4 are zero to twelve amino acids. A disulfide bond between the cysteine residues of the segment Cys Val Gly Cys and an amino-terminal and/or carboxy-terminal protecting group are optionally present;

(2) A pharmaceutical composition comprising a compound with the formula X5 Leu Asp X7 Asn Ala Glu Val Tyr X8 (C), where X5 and X6 are zero to twelve amino acids, X7 is Ala or Cys, and the compound optionally contains an amino-terminal and/or carboxy-terminal protecting group;

(3) A pharmaceutical composition comprising a peptide fragment of high molecular weight **kininogen** domain 3 or an analog where cysteine residues are replaced by alanine residues that **inhibits** endothelial cell proliferation. The fragment optionally contains an amino-terminal and/or carboxy-terminal protecting group;

(4) **Inhibiting angiogenesis** comprising administering to a mammal the new composition;

(5) **Inhibiting** endothelial cell proliferation comprising administering to a mammal the new composition;

(6) Inducing endothelial cell apoptosis comprising administering to a mammal the new composition;

(7) **Inhibiting** endothelial cell proliferation comprising contacting endothelial cells with a compound of formula (A), (B) or (C);

(8) **Inhibiting** endothelial cell proliferation comprising contacting endothelial cells with a peptide fragment of high molecular weight **kininogen** domain 3 or an analog where cysteine residues are replaced by alanine residues. The compound optionally contains an amino-terminal and/or carboxy-terminal protecting group.

ACTIVITY - Anti-angiogenic; Cytostatic; Antirheumatic; Antiarthritic;

Ophthalmological. The median **inhibitory** concentrations for 6 of the claimed sequences were less than 0.8 to 28 micro M for fibroblast growth factor-induced endothelial cell proliferation of 30000 cells/ml

human umbilical vein endothelial cells.

MECHANISM OF ACTION - **Kininogen** domain 3 anal

USE - The new composition is used to **inhibit angiogenesis, inhibit** endothelial cell proliferation or induce endothelial cell apoptosis (claimed). Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

Dwg.0/0

ACCESSION NUMBER: 2000-442247 [38] WPIDS

DOC. NO. CPI: C2000-134415

TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis,

and ocular disorders comprises a **kininogen** domain 3 analog.

DERWENT CLASS: B04 D16

INVENTOR(S): MCCRAE, R K

PATENT ASSIGNEE(S): (MCCR-I) MCCRAE R K; (UTEM) UNIV TEMPLE

COUNTRY COUNT: 89

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000035407	A2	20000622	(200038)*	EN	44
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL					
OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES					
FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS					
LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ					
TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000017494	A	20000703	(200046)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000035407	A2	WO 1999-US28465	19991202
AU 2000017494	A	AU 2000-17494	19991202

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000017494	A Based on	WO 200035407

PRIORITY APPLN. INFO: US 1998-112427 19981216

L7 ANSWER 95 OF 95 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

TI A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis.

AN 2000-376483 [32] WPIDS

AB WO 200027866 A UPAB: 20000706

NOVELTY - A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis, is new.

DETAILED DESCRIPTION - A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of the formula (I) and optionally comprises an amino terminal and/or carboxy terminal protecting group, is new:

(I) X1-His-Lys-X-Lys-X2;

X = any amino acid;

X1 = 0-12 amino acids; and
X2 = 0-12 amino acids.
INDEPENDENT CLAIMS are also included for:
(1) a method of **inhibiting angiogenesis** comprising administering to a mammal an effective amount of (I);
(2) a method of **inhibiting** endothelial cell proliferation comprising administering to a mammal an effective amount of (I);
(3) a method of inducing endothelial cell apoptosis comprising administering to a mammal an effective amount of (I);
(4) a method of **inhibiting angiogenesis** comprising administering to a mammal an effective amount of two-chain high molecular weight **kininogen**;
(5) a method of **inhibiting** endothelial cell apoptosis comprising administering to a mammal an effective amount of two-chain high molecular weight **kininogen**;
(6) a method of **inhibiting angiogenesis** comprising administering to a mammal an effective amount of single chain high molecular weight **kininogen**;
(7) a method of **inhibiting** endothelial cell proliferation comprising contacting endothelial cells with (I); and
(8) a compound of formula (i) and optionally comprising an amino terminal and/or carboxy-terminal protecting group. :
(i) X1-His-Lys-X-Lys-X2:
X1 = His-Gly-His-Glu-Gln-Gln-His-Gly-Leu-Gly-His-Gly or N-terminal truncation fragment thereof containing at least one amino acid;
X2 = 0 amino acids or the segment Leu-Asp-Asp-Leu-Glu-His-Gln-Gly-Gly-His-Val, or C-terminal truncation fragment thereof containing at least one amino acid.
ACTIVITY - None given.
MECHANISM OF ACTION - None given.
USE - (I), a two-chain high molecular weight **kininogen**, or a single chain high molecular weight **kininogen** can be used in methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation and for inducing endothelial cell apoptosis (claimed).
ADVANTAGE - None given.
Dwg.0/8
ACCESSION NUMBER: 2000-376483 [32] WPIDS
DOC. NO. NON-CPI: N2000-282694
DOC. NO. CPI: C2000-113885
TITLE: A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): MCCRAE, R K
PATENT ASSIGNEE(S): (MCCR-I) MCCRAE R K; (UTEM) UNIV TEMPLE
COUNTRY COUNT: 89
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000027866	A1	20000518	(200032)*	EN	52
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL					
OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES					
FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS					
LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ					
TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000019106	A	20000529	(200041)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000027866	A1	WO 1999-US26419	19991105
AU 2000019106	A	AU 2000-19106	19991105

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000019106	Based on	WO 200027866

PRIORITY APPLN. INFO: US 1998-107833 19981110